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DISTURBANCES IN SLEEP MECHANISM: A CLINICO-PATHOLOGIC STUDY

I. LESIONS AT THE CORTICAL LEVEL

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Disturbances in sleep consisting of insomnia or hypersomnia can be divided into three main groups: those associated with lesions of the nervous system, those caused by use of drugs and those of psychogenic origin. In this presentation we shall be concerned essentially with hypersomnia caused by lesions of the central nervous system. Although this topic has been the subject of numerous contributions, the material under observation justifies a revaluation of this interesting problem. Attempts to explain the mechanism concerned in disturbances of sleep in man on a neuroanatomic and physiologic basis have led to various interpretations. The problem is beset with difficulties because the lesions in many of our cases and in those reported by other investigators were neither single nor limited to specific areas in the nervous system. This is especially true when the somnolence is associated with cerebrovascular lesions or diseases with bilateral or multiple lesions of the central nervous system. It is not always possible to state with certainty that a localized lesion due to a neoplasm is the cause of this physiologic deviation because there may be a widespread disturbance in function through compression of other structures or through interference with the cerebrospinal circulation. A careful evaluation, however, of the clinical symptoms and the location of the significant lesion may aid in proving which centers and pathways are responsible for hypersomnia or insomnia.

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As will be demonstrated, disturbances in sleep may occur with lesions at various levels of the nervous system, from the cortex to the medulla oblongata.

There is some experimental evidence in the human subject indicating the probable site of the responsible lesion. Disturbances of sleep in patients with involvement of the hypothalamus, either by neoplasm or secondary to encephalitis lethargica, indicates the importance of this center. Although the hypothalamus seems to be the main center controlling sleep, it is well to remember that it is in intimate connection with the cortex, the thalamus, the basal ganglia, the mesencephalon and the brain stem. A lesion in any of these centers or in the connecting pathways may result in disturbance of integration of the sleep mechanism. The disintegration of this mechanism may be caused by destructive and irritative lesions, as well as by psychogenic factors. The disturbances of a psychologic nature may also depend on interference with the centers and pathways, to be described. In several of the cases included in this presentation there were slight psychotic or neurotic phenomena. Despite their presence, psychologic and neurologic examinations showed that the disturbance of sleep was organic in nature.

From the nosologic point of view, disturbances in sleep should include the various common designations: lethargy, somnolence, stupor, coma and unconscious states. Some observers believe these to be separate entities rather than phases or stages of the same dysfunction, regulated by identical centers and pathways. They assert that hypersomnia or somnolence should be differentiated from stupor, for in the former the patient can easily be aroused and when awakened appears to be in complete possession of his senses. Some observers claim that encephalitic patients when awakened are promptly oriented and that

their consciousness appears unclouded. Others maintain, however, that somnolence or lethargy, as best seen in cases of encephalitis, varies from slight drowsiness to complete stupor. Our experience and the observations of many other investigators indicate that in a number of cases of encephalitis the patients cannot be aroused completely from their lethargy. Disturbances of sleep and consciousness leading to stupor, coma and other unconscious states are probably closely related. They are the result of lesions in those parts of the central nervous system concerned with the sleep mechanism. A lesion in these centers or in their connections may disturb not only sleep but consciousness. It is therefore not unusual to find in such cases not only pure pathologic sleep but a certain amount of stupor and coma. The analysis of our material does not justify clearcut differentiation of sleep, unconscious states, stupor and coma.

About 300 cases of disturbances in the sleep mechanism were observed clinically, and autopsies were performed in 57 cases. Most of the deaths were due to neoplasms; the remainder resulted from vascular or other diseases of the nervous system. The 57 cases in which autopsy was performed and the 2 cases in which the diagnosis was verified at operation and which were included in this presentation were studied fully in order to determine the location of the lesion. A number of cases in which diffuse lesions existed in the cortex, diencephalon, mesencephalon and metencephalon were omitted from this presentation, for their inclusion would have been confusing from the point of view of localization.

Location of Lesions	No. of Cases
Cortical	9
Corticodiencephalic	25
Diencephalic (hypothalamus)	17
Mesencephalic-metencephalic	8
	59

METHOD OF PROCEDURE

Every patient reported on was observed during the period of disturbance of sleep. A number of questions were asked, and attempts were made to arouse the patient, as indicated in the brief history of each case. The few patients in deep coma who could not be aroused were not included in this study. Since many observers believe that such factors as increased intracranial pressure, endocrine disturbances and ocular manifestations play an important part in disturbances of sleep, special attention was given to these features in order to evaluate their significance. Only the pertinent facts regarding disturbances in sleep will be given in the report of these cases.

Each brain was sectioned coronally or horizontally at intervals of 1 cm., so that lesions of significant size were not missed. In all instances blocks from the areas of destruction or of the tumor, and from the tissue above and below them, were embedded in pyroxylin and stained by the myelin sheath and the cresyl violet method. In many cases entire sections of the brain were embedded in pyroxylin and cut serially at a thickness of 50 microns. The hypothalamic region was studied by the same methods in all cases.

LESIONS AT THE CORTICAL LEVEL

The ability of man to fall asleep voluntarily is an indication that the sleep mechanism is under the regulation of higher cortical centers. It is therefore reasonable to assume that disturbances of cortical function have some influence on abnormal sleep. The awakening of a patient from lethargy and mental cloudiness, as seen in cases of lethargic encephalitis and other diseases of the central nervous system, and his response to questions are further evidence that the higher psychic centers play an important role in the regulation of sleep. The cases of psychogenic sleep furnish additional proof of cortical influence on sleep. Psychogenic disturbances in sleep, which probably have their origin in the cortex, are most likely mediated by way of the corticohypothalamic pathways. In our cases in which lesions existed at the cortical level, we postulate that involvement of the aforementioned centers or tracts removed the normal regulatory control of the cortex over the hypothalamus.

This report is concerned with 9 cases of disturbances of sleep in which the lesion was entirely restricted to the cerebral cortex and white matter.

REPORT OF CASES

CASE 1.—*Infrafrontal meningioma: somnolence and unconsciousness. No clinical evidence of increased intracranial pressure.*

G. C., a woman aged 80, had sudden onset of paralysis of the left side, associated with somnolence, followed by unconsciousness, from which she could be aroused. Later she regained consciousness and began to move the paralyzed extremity.

Neurologic Examination.—Examination disclosed diminished reflexes bilaterally, absence of pathologic reflexes, loss of vision and secondary optic nerve atrophy in the right eye. The patient was dull and apathetic, with periods of somnolence.

Laboratory Data.—The urine and blood chemistry were normal. Lumbar puncture was not performed.

Autopsy.—There was a large, encapsulated meningioma situated between the two frontal convolutions, destroying the greater part of the white matter of all the frontal convolutions and leaving only a thin shell of gray matter (fig. 1). The tumor did not extend posteriorly beyond the tips of the anterior horns of the lateral ventricles. The diencephalon was not compressed, and the hypothalamic nerve cells stained normally.

The tumor in this instance did not compress the hypothalamus. The loss of vision in the right eye was the result of compression of the right optic nerve.

CASE 2.—*Chondrosarcoma of the right frontal convolutions: somnolence and, toward the end, semistupor. Evidence of increased intracranial pressure.*

G. S., a boy aged 13 years, gave a history of projectile vomiting, followed shortly by diplopia and headache. Thereafter he became drowsy but could be aroused.

Neurologic Examination.—Examination at this time revealed an abnormal amount of hair; large genitalia and an undescended left testicle; large head, hands and feet, and scoliosis. There were anosmia, bilateral papilledema, with secondary optic nerve atrophy, and weakness of the right side of the face of central type. The presence of a pinealoma was suspected, and roentgen therapy was instituted.

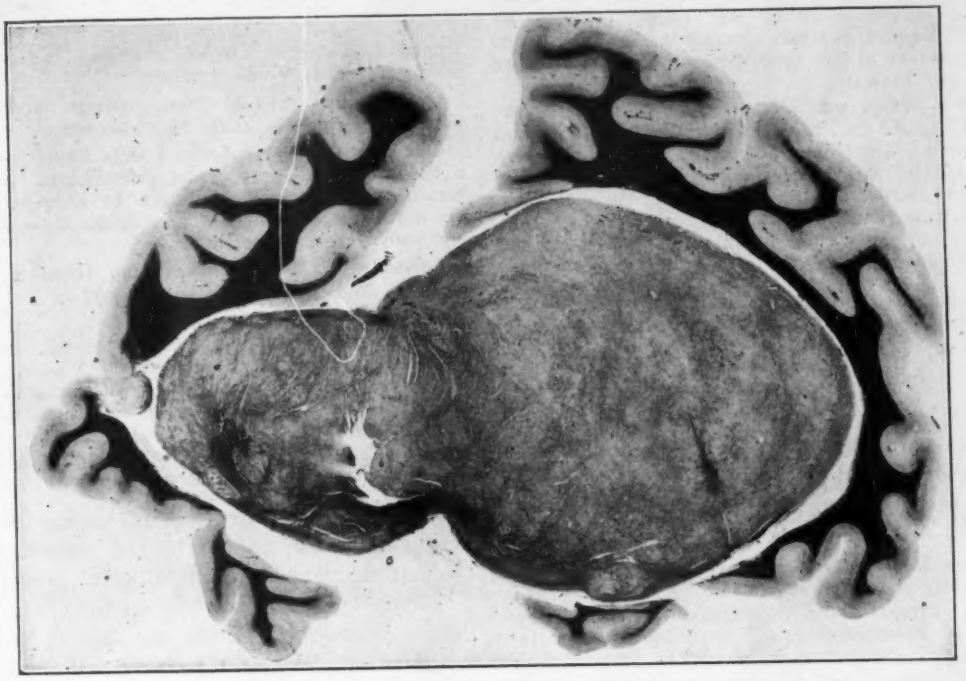

Fig. 1 (case 1).—Infrafrontal meningioma.

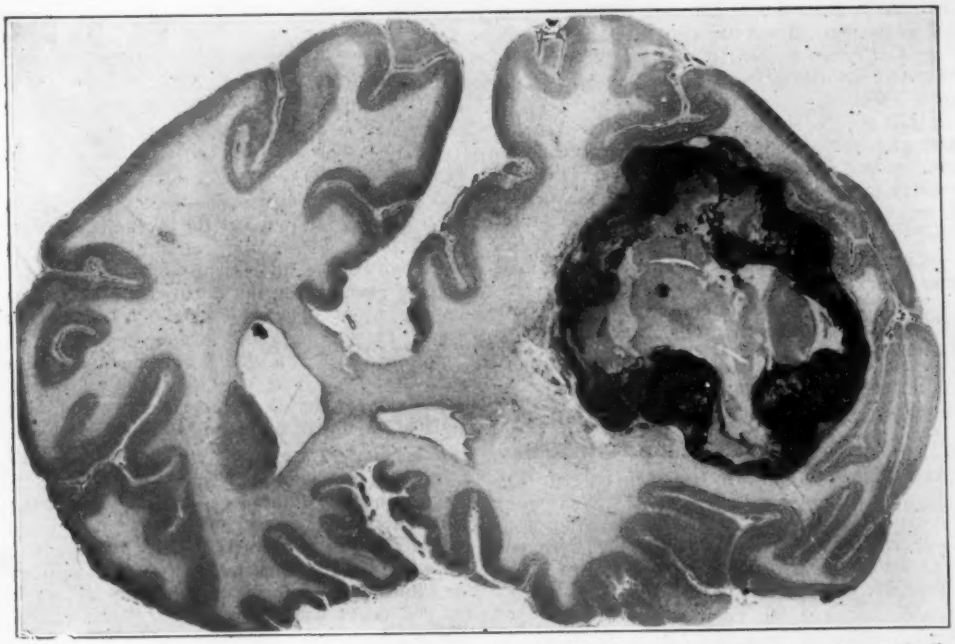

Fig. 2 (case 2).—Chondrosarcoma of the right frontal convolutions. Notice compression and distortion of the tip of the right lateral ventricle.

Laboratory Data.—The spinal fluid was under an initial pressure of 400 mm. of water; it was clear and contained 3 cells per cubic millimeter.

Course.—After roentgen therapy the drowsiness disappeared; the patient became well adjusted, attended

school at the hospital and entertained himself by listening to recordings of many of the classics in literature. Two years later there developed a hard mass in the right frontal bone, aspiration of which revealed a chondrosarcoma. The boy became increasingly drowsy and somnolent. In the early stages he could easily be aroused when he was loudly spoken to or prodded. The drowsiness increased to semistupor. Spinal puncture at this time showed an initial pressure of 440 mm. of water.

Autopsy.—There was a large cauliflower mass, measuring 4.5 by 3.5 cm., in the dura over the right frontal convolutions. The frontal and motor convolutions were compressed by this neoplasm (fig. 2). Part of the second and third frontal convolutions of the right side were destroyed and infiltrated by the tumor. The nerve cells of the various hypothalamic nuclei did not show pathologic changes.

The lesion in this instance was essentially cortical (frontal). Of interest is the disappearance of the lethargy after high voltage roentgen therapy. Interference with hypothalamic function can be ruled out, for pathologic changes could not be demonstrated in the hypothalamus. The presence of diplopia in this case, alone of the group with cortical lesions, may have been the result of the increased intracranial pressure.

CASE 3.—*Meningiomas compressing the right frontal convolutions; somnolence; mental impairment. Evidence of increased intracranial pressure. Removal of tumor and disappearance of somnolence and other symptoms.*

L. Y., a woman aged 43, complained of increasingly severe headaches, somnolence and weakness.

Neurologic Examination.—There were bilateral papilledema and drowsiness, from which the patient could be aroused. There was marked impairment of memory, with considerable disorientation and blocking of thought.

Laboratory Data.—The spinal fluid showed an initial pressure of 230 mm. of water. There was a trace of albumin and globulin, and the total protein content was 43 mg. per hundred cubic centimeters. The urine and blood chemistry were normal. Ventriculographic studies suggested an expanding lesion of the right frontal region.

Course.—Craniotomy was performed, and two small meningiomas over the right frontal convolutions were removed. After the operation the somnolence disappeared. The patient remained well about five years after operation.

The evidence that the patient recovered from the somnolence after removal of the meningiomas from the frontal convolutions indicates that this cortical area plays a role in the control of the sleep mechanism.

CASE 4.—*Hemangioma compressing the right frontal convolutions; lethargy. No evidence of increased intracranial pressure.*

C. S., a woman aged 60, complained of headache and drowsiness, which progressed to lethargy.

Neurologic Examination.—The patient was continuously drowsy but could be awakened at times. Sometimes she lapsed into deep stupor. There was no papilledema or other abnormal neurologic sign.

Laboratory Data.—The blood chemistry was normal. The cerebrospinal fluid was under a pressure of 130 mm. of water; the total protein content was 25 mg. per hundred cubic centimeters.

Autopsy.—There were multiple telangiectatic hemangiomas of the liver, the frontal bones and the vertebral bodies. In the right frontal bone a circular area, 3 cm. in diameter, blue-black, compressed the frontal convolutions. The hypothalamic nuclei and their nerve cells were normal.

CASE 5.—*Subdural hematoma compressing the left frontal convolutions; lethargy ending in coma. No increase in intracranial pressure.*

G. J., a boy aged 15 years, suffered from drowsiness, from which he could be awakened.

The only neurologic findings were hyperreflexia and a Babinski sign on the right side. Later the patient became comatose and could not be aroused. Before his death, the left pupil became larger than the right, and both were fixed to light.

Laboratory Data.—A spinal tap revealed xanthochromic fluid, with an initial pressure of 140 mm. of water.

Autopsy.—There was thickening of the dura, with a subdural hematoma on the left side compressing the frontal, motor and temporal convolutions. The pia-arachnoid was slightly adherent and thickened. The anterior horn of the left lateral ventricle was constricted, distorted and pushed to the right. The hypothalamic nuclei and their nerve cells were normal.

In this case the drowsiness, ending in coma, undoubtedly was caused by the compression of the left hemisphere, especially the frontal convolutions. Except for the slight distortion in the anterior horn of the left lateral ventricle, there was no evidence of increased intracranial tension.

CASE 6.—*Glioblastoma multiforme of the right cerebral hemisphere, extending from the frontal to the occipital convolutions, slightly compressing, but not invading, the superior part of the diencephalon; lethargy. No evidence of increased intracranial pressure.*

S. A., a man aged 59, gave a history of "dozing off" at frequent intervals.

Neurologic Examination.—There was left hemiplegia with signs of injury to the pyramidal tract and loss of all forms of sensation on the left side. The fundi were normal. The patient fell asleep frequently during the examination but could easily be awakened when spoken to loudly or shaken. When awakened, he would answer questions properly. At times he was confused and disoriented. This mental state was most pronounced when he was lethargic but would clear up if he was awakened or, interestingly, if a pretty nurse assisted in the examination.

Laboratory Data.—All examinations, including urinalysis, gave essentially normal results. The urea nitrogen of the blood measured 25 mg. per hundred cubic centimeters. The cerebrospinal fluid was under a pressure of 200 mm. of water, but the patient was straining at the time. The total protein content of the fluid was 67 mg. per hundred cubic centimeters; the cell count was normal. The Wassermann reaction was negative.

Autopsy.—There was a glioblastoma multiforme of the right hemisphere extending from the frontal to the occipital convolutions, including the gyrus cingulus on the right side and part of the corpus callosum on the left side (fig. 3). The right lateral ventricle was distorted and constricted. The hypothalamus was not invaded, but the superior part on the right side was slightly compressed (fig. 3). Sections through various

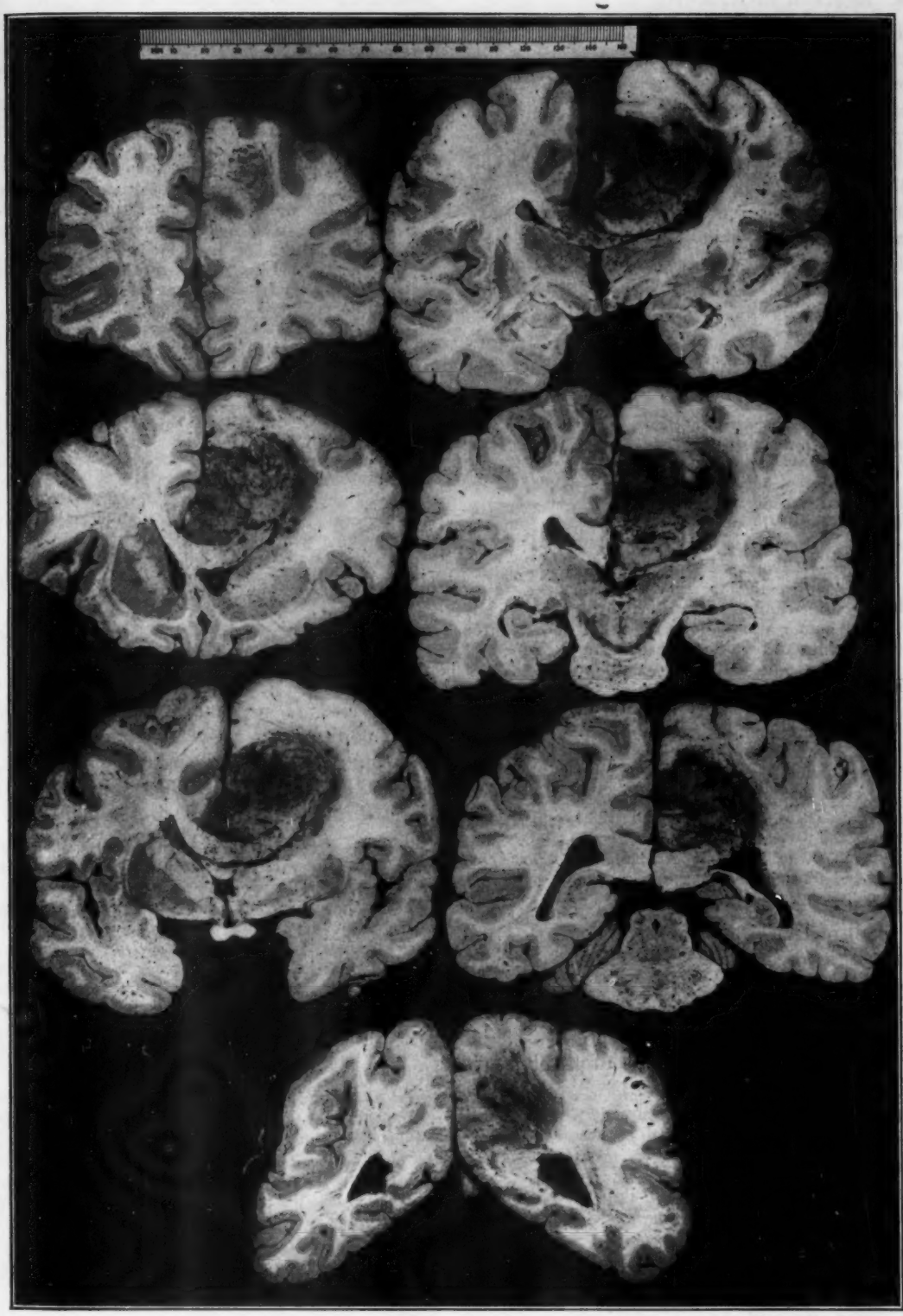

Fig. 3 (case 6).—Glioblastoma multiforme of the right hemisphere, extending from the frontal to the occipital convolutions and including the gyrus cingulus. Notice the slight compression of the right lateral ventricle and the superior part of the right hypothalamus, with absence of invasion.

regions of the hypothalamus did not disclose any pathologic changes in its nerve cells.

The tumor in this case was essentially limited to the cortex, with slight compression of the superior part of the right hypothalamus. However, there were no changes in the hypothalamic nerve cells. There was no significant evidence of increased intracranial pressure, either clinically or pathologically. The initial pressure of 200 mm. of water was the result of poor relaxation of the patient, which, according to Friedman and Merritt [1] and others, may be disregarded. In this instance, the right gyrus cingulus was also invaded by the neoplasm. This area, as suggested by Papez,[2] plays some role in emotional disturbances and may also be concerned with the function of sleep.

CASE 7.—*Spongioblastoma polare of the left motor and parietal region; somnolence. Clinical evidence of slight increase in intracranial pressure.*

S. H., a woman aged 60 had spontaneous pain in the right upper extremity, dizziness, nausea and vomiting, paralysis of the right upper and lower extremities and aphasia.

Neurologic Examination.—Examination disclosed hemiparesis with pathologic reflexes and a hemisensory syndrome on the right side, bitemporal pallor of the optic disk, psychomotor retardation and depression. In the last two months of her illness the patient slept most of the time. She was not able to speak but answered questions by gestures when awakened.

Laboratory Data.—The blood chemistry was normal. The cerebrospinal fluid was under a pressure of 110 mm. of water. The reaction for globulin was 1 plus, and the total protein content of the spinal fluid was 62 mg. per hundred cubic centimeters.

Autopsy.—There was a spongioblastoma polare in the left motor and parietal regions. It extended slightly into the centrum ovale. The hypothalamus was not compressed, and the hypothalamic nuclei did not show any pathologic changes.

The disturbance of sleep in this case was the result of involvement of the cortex, as there were no changes in the hypothalamus. Although the spinal fluid pressure was normal, the changes in the optic disks were considered to be secondary to increased intracranial pressure.

CASE 8.—*Meningioma of the right parieto-occipital convolutions, with peculiar disturbances of sleep. Clinical evidence of increased intracranial pressure. Questionable compression of the hypothalamus, without pathologic changes.*

R. S., a woman aged 48, sustained an injury to the back of her head during a fall. One year later she complained of failing vision, weakness and headaches. At this time she began to have peculiar disturbances of sleep. She would go to sleep about 6 p. m., awaken at 2 a. m., fall asleep again within an hour and then reawaken at 7 a. m. Soon afterward she would fall asleep again and sleep a great part of the day. She could easily be aroused but would soon lapse into sleep again.

Neurologic Examination.—Examination revealed a large mass over the right occipital bone, bilateral papilledema with suggestive left homonymous hemianopsia and conjugate deviation of the head and eyes to the right. There was hyperreflexia on the left side. The patient was confused and rambled continuously when awakened, until she fell asleep again.

Laboratory Data.—Roentgenographic examination of the skull disclosed a circumscribed area of destruction of bone in the right occipital and parietal regions the size of a lemon, with radiating spicules of ossification. The urea nitrogen of the blood was normal. The cerebrospinal fluid was under a pressure of 115 mm. of water; the fluid was clear and contained no cells.

Course.—The extracranial and intracranial portions of the tumor were removed at two separate operations. The tumor extended to the sagittal suture and compressed the opposite occipital lobe. The patient went into shock and died.

Autopsy.—Part of the bone in the righ parieto-occipital region was destroyed by the invading meningioma. The tumor was situated over the right parieto-occipital lobes, causing extensive destruction of the superior parietal, the angular and part of the first occipital convolution and compressing the occipital convolutions on the opposite side. The ventricles on the right side were constricted and distorted. There was questionable compression of the diencephalic nuclei, but the nerve cells of the hypothalamus appeared normal.

This case is of interest because of the peculiarity in the disturbance of sleep in which the patient slept a great part of the day and had short periods of awakening. Although the cerebrospinal fluid pressure was within normal limits, the papilledema and the constriction of the ventricular system indicated increased intracranial pressure.

CASE 9.—*Pachymeningitis hemorrhagica interna, compressing the right frontoparietal convolutions; somnolence. No evidence of increased intracranial pressure.*

F. J., a man aged 49, complained of headache, weakness, hiccuping, yawning and drowsiness. When he was drowsy, and sitting, his head would sag and turn to the right, and he would fall asleep. When awakened he would answer questions coherently for a short time and then promptly fall asleep again. Thirty years previously he had had a syphilitic infection, for which he received treatment. There was no history of head injury or of alcoholism.

Neurologic Examination.—The patient was extremely somnolent and yawned frequently; there was spastic hemiparesis with pyramidal tract signs on the left side; the pupils were irregular, and the left one was fixed to light and in accommodation; there was no papilledema. The patient exhibited mental deterioration and poor orientation.

Laboratory Data.—The Wassermann reactions of the blood and the spinal fluid were 4 plus. The cerebrospinal fluid was under a pressure of 80 mm. of water. The urine was normal, and the urea nitrogen of the blood was within normal limits.

Course.—The patient became progressively more drowsy, lapsed into coma and died. The temperature ranged between 97 and 98 F. for four weeks, and once it was 96.4 F.

1. Friedman, A. P., and Merritt, H. H.: Personal communication to the authors.

2. Papez, J. W.: A Proposed Mechanism of Emotion, Arch. Neurol. & Psychiat. **38**:725 (Oct.) 1937.

Autopsy.—The outer surface of the dura over the right frontomotor and parietal region was extensively thickened and contained an organized hematoma. The right frontal, motor and parietal convolutions were flattened. There was a slight constriction of the right lateral ventricle. Sections of the dura disclosed a typical picture of pachymeningitis hemorrhagica interna. There was a slight meningeal reaction. No inflammatory process was noted in the cortex. The hypothalamus was not compressed, and its nerve cells were normal.

The somnolence in this case was caused by compression of the right frontal, motor and parietal convolutions.

COMMENT

Experimentally there is little evidence that pure cortical lesions cause disturbances in the sleep mechanism, although Sager [3] and Neiwenhuyzen [4] produced catalepsy in the cat after decortication. Johnson [5] spoke of special "sleep" neurons in the cerebral cortex since sleep shows the patterns of learning by experience and habit formation and these features are characteristic of cortical activities. According to him, catabolic products activate the sleep neurons, which inhibit the other cortical neurons. He stated the belief that "the relations between the sleep system and the whole of the central nervous system, concerned only in elaborating the reactions of the waking state, are mutually antagonistic."

Pathologic sleep, chiefly in the form of hypersomnia, had been known to occur in cases of pure cortical neoplasms. In some of these cases it was difficult to rule out the role played by secondary compression of the hypothalamus and the effect of the generalized increase in intracranial pressure. It is well to bear in mind that a neoplasm, no matter how small, will interfere to some degree with the circulation of the cerebrospinal fluid. Righetti,[6] in 1903, analyzed the histories of 775 patients with tumors of the central nervous system. Of these, 115 had pathologic sleep. In 6 per cent of the latter the neoplasms were situated in the frontal lobe. Léchelle, Alajouanine and Thévenard [7] reported 2 cases of tumor of the frontal lobe, with hypersomnia as the main symptom in 1 case and as the only symptom in the other. They asserted that somnolence is the predominant symptom of tumors of the frontal lobe. Kolodny [8] investigated 38 cases of tumors of the temporal lobe and found hypersomnia in 9. Frazier,[9] in a collection of 105 cases of tumors of the frontal lobe, noted some form of hypersomnia, ranging from drowsiness to stupor, in 34. He regarded somnolence as a neighborhood symptom and as secondary to involvement of the diencephalon. He stated the opinion that sleepiness may be due to increased intracranial pressure, within the third ventricle particularly. McKendree and Feinier [10] analyzed 100 cases of cerebral neoplasms and found somnolence most constantly when there was pronounced internal hydrocephalus. The absence of somnolence in many other cases of pure cortical lesions with evidences of increased intracranial pressure militates against the view that increased intracranial tension may cause or be the sole basis of disturbances in the waking center or centers. It seems likely that the role played by increased intracranial pressure in dysfunction of sleep is somewhat overestimated. In a review of 328 cases of tumors of the central nervous system in which necropsy was performed, evidence of increased intracranial pressure was present in about 70 per cent; yet disturbances of sleep occurred only in 18 per cent. The percentage of cases of increased intracranial pressure in our series of cases of disturbances of sleep was also about 70 per cent.

Of about 60 cases of pathologic sleep associated with a lesion of the central nervous system, a solitary cortical lesion was found in 9. In none of these cases was the hypothalamus invaded; in 2 instances compression of the hypothalamus could not be completely ruled out. In 5 cases (1, 4, 5, 6 and 9) there was no clinical or manometric evidence of increased intracranial pressure. In 4 cases (2, 3, 7 and 8) there was increased intracranial pressure, and the role played by this factor in dysfunction of sleep cannot be absolutely ruled out. In case 1 manometric studies were not done, but there was no clinical evidence for increased intracranial tension. In cases 7 and 8 the manometric readings were normal, but there was clinical evidence of increased intracranial tension. The

3. Sager, O.: Experimentelle Untersuchungen über die Bulbocapninstarre, Ztschr. f. d. ges. exper. Med. **81**: 543, 1932.

4. Niewenhuyzen, F. J.: Etude sur la localisation des phénomènes cataleptiques chez le chat, Acta brev. Neerland. **4**:89, 1934.

5. Johnson, G. T.: Sleep as a Specialized Function, J. Abnorm. & Social Psychol. **18**:88, 1923.

6. Righetti, R.: Contributo clinico ed anatomopatologica alla studio die gliomi cerebrali, Riv. di pat. nerv. **8**:24, 1903.

7. Léchelle, Alajouanine and Thévenard: Deux cas de tumeur du lobe frontal à forme somnolente, Bull. et mém. Soc. méd. d. hôp. de Paris **49**:1347, 1925.

8. Kolodny, A.: The Symptomatology of Tumors of the Temporal Lobe, Brain **51**:385, 1928.

9. Frazier, C. H.: Tumors Involving the Frontal Lobe Alone, Arch. Neurol. & Psychiat. **35**:525 (March) 1936.

10. McKendree, C. A., and Feinier, L.: Somnolence, Arch. Neurol. & Psychiat. **17**:44 (Jan.) 1927.

most definite criteria for clinical evidence of increased intracranial tension considered by us were papilledema and projectile vomiting; all other symptoms are questionable. Manometric evidence of increased intracranial tension consisted of an initial pressure of 200 mm. or above with the patient relaxed and in the lateral recumbent position. Diplopia was present in only 1 case. There were no endocrine disturbances, except in a boy of 13 (case 2), in whom the presence of a pinealoma was suspected and who had an abnormal amount of hair, large genitalia and large hands and feet. Slight deviations from the normal temperature were present only in case 9. In 1 case the removal of a meningioma from the right frontal area resulted in disappearance of the somnolence.

From our series of cases of pure cortical lesions, and from the cases reported by other authors, we are of the opinion that some fibers for the control of sleep may originate in the cerebral cortex, especially the hippocampal, cingular, frontal, premotor and temporal lobes. Bard's [11] experiments on sham rage indicate that the hypothalamus is to some degree under the control of the cerebral cortex. These impulses, such as occur in affective states for the expression of emotion and feelings (Davison and Kelman [12] and others), are mediated by voluntary and involuntary pathways, probably controlled by the corticohypothalamic pathways. The voluntary efferent impulses are possibly mediated via the pyramidal pathways. This subject will be discussed in greater detail in a subsequent presentation.

Somnolence is infrequently observed in cases of pure cortical lesions, except when these are fairly extensive, because the neurons and pathways controlling sleep are widely scattered and are not concentrated in one small area, as are the same structures in the hypothalamus. It is well known that a complete hemiplegia is more likely to occur with a small lesion of the internal capsule than with a small cortical lesion. Similarly, disturbances in sleep are more likely to occur as a result of hypothalamic than of cortical lesions.

Cranial trauma may also lead to total loss of consciousness or to lethargy. In some instances the patient can be awakened; in others, not. These cases cannot be cited as proof of cortical control, for in most instances there was interference with cerebrospinal pressure; moreover, the lesions were usually widespread and probably involved the hypothalamus.

SUMMARY AND CONCLUSIONS

In 9 cases pathologic sleep was associated with lesions in the cortex. In none was there invasion of the hypothalamus. In 2 cases compression of the hypothalamus could not be completely ruled out. On microscopic examination, however, there was no evidence of changes in the nerve cells.

Increased intracranial pressure was present in only 4 of the 9 cases. It is reasonable to assume that the role played by increased intracranial tension in dysfunction of sleep is negligible, if not totally insignificant. Ocular and endocrine disturbances, except for diplopia in 1 case and endocrine features in another, were absent in this group of cases.

From the study of this series of cortical lesions, we are of the opinion that some fibers for the control of sleep originate in the cerebral cortex, especially the hippocampal, cingular, frontal, premotor and temporal convolutions. These areas are connected with the hypothalamus by means of the corticohypothalamic pathways. Injury to these areas or to their connections with the hypothalamus is occasionally the cause of pathologic sleep.

Montefiore Hospital for Chronic Diseases.

11. Bard, P.: A Diencephalic Mechanism for the Expression of Rage with Special Reference to the Sympathetic Nervous System, Am. J. Physiol. **84**:490, 1928.

12. Davison, C., and Kelman, H.: Pathological Laughing and Crying, Arch. Neurol. & Psychiat. **42**:595 (Oct.) 1939.

DENIAL OF BLINDNESS BY PATIENTS WITH CEREBRAL DISEASE

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Occasional cases of denial of blindness or deafness in cases of focal cerebral disease have been reported in the French, Russian and German literature but have received hardly any attention from Anglo-Saxon authors. However, denial of blindness in cases of pathologic conditions of the brain is frequent, although overlooked by most observers. Here, 6 cases of denial of blindness will be reported, the literature reviewed and the syndrome discussed.

REVIEW OF LITERATURE

In 1896 Anton gave a verbal report of a case with bilateral softenings of the visual radiations, followed by complete blindness which the patient himself did not notice. Anton wrote two papers,[1] in which he reported this case and 3 others. The first case was that of a 56 year old seamstress who was amaurotic but unaware of her blindness. She had dysphasia of the amnestic type; otherwise the results of neurologic examination were essentially normal. She did not appear to be very deteriorated. Spatial orientation was impaired, and she was unable to localize voices or to estimate distances by hearing. Autopsy revealed bilaterally symmetric lesions of the angular gyrus and the first and second occipital gyri, involving the medullary substance, and a small lesion in the splenium of the corpus callosum. The second case was that of a 64 year old teamster who was completely deaf but thought he could hear well. The patient often complained that others made such a noise that he could not follow the conversation. It appeared as though he had auditory hallucinations but he never answered questions or expected answers to his own questions. He was friendly and seemed oriented. He had dyslexia and dysgraphia. The results of neurologic examination were otherwise normal. There was no marked deterioration. Later paranoid delusions developed. No autopsy is reported. The clinical diagnosis was bilateral softening of the temporal lobes. The third case was that of a 69 year old female dairy worker who was admitted in a state of excitement and confusion with sensory aphasia. The patient was unaware of her inability to understand spoken words. Autopsy revealed bilateral destruction of the first and second temporal gyri, extending toward the occipital lobes. Anton stressed the destruction of the association fibers between the occipital, temporal and lower parietal lobes. He concluded that the syndrome of denial of sensory deficiency due to cerebral lesions is caused by destruction of the association tracts. He described clearly that such a syndrome is not due to deterioration, hallucinations or hysterical manifestations. Actually, only his first case constitutes what later was referred to as Anton's syndrome.

Careful combing of the literature revealed that the syndrome had been described before Anton, but only in a casual manner, usually with stress on other features of the case. Von Monakow [2] described 2 cases. The first was that of a 70 year old man with left hemiplegia and slight aphasic disturbances. The patient was not greatly deteriorated. He was blind but was unaware of his blindness. Often he thought that he was in a dark hall. Autopsy showed old and recent bilateral softenings in the cuneus and the lingular gyrus, extensive areas of encephalomalacia of the left occipital lobe and both superior temporal gyri and softenings in the right thalamus and the right lateral geniculate body. The second case was that of a 50 year old man with epileptic seizures in whom bilateral hemianopsia developed. He had amnestic aphasia and was disoriented. Spatial orientation and memory for the appearance of objects were impaired. He was totally unaware of his blindness. Autopsy showed recent bilateral

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1. Anton, G.: (*a*) Ueber die Selbstwahrnehmung der Herderkrankungen des Gehirns durch den Kranken bei Rindenblindheit und Rindentaubheit, Arch. f. Psychiat. **32:** 86-127, 1899; (*b*) Ueber Herderkrankungen des Gehirns, welche vom Patienten selbst nicht wahrgenommen werden, Wien. klin. Wchnschr. **11:**227-229, 1898.

2. von Monakow, A.: Experimentelle und pathologisch-anatomische Untersuchungen über die Beziehungen der sogennanten Sehspäre zu den infracorticalen Opticuscentren und zum Nervus opticus, Arch. f. Psychiat. **16:** 151-199, 1885.

softenings of the cuneus and the lingular gyrus and old softenings in the third frontal gyrus. Dejerine and Vialet [3] reported the case of a 64 year old man who had two apoplectic attacks, the second followed by complete and sudden blindness. The patient walked like a blind man but did not realize his blindness; he called objects by false names and said tears were in his eyes. Autopsy showed an area of old encephalomalacia in the cuneus and lingular gyrus on the right side, extending toward the occipital pole, and fresh softenings of the calcarine and the lingular gyrus on the left side. Rossolimo [4] reported the case of a patient who was totally blind and did not recognize it. Autopsy revealed a softening in the cuneus and the lobus lingualis on the left side involving most of the white matter. There was a massive hemorrhage of the basal ganglia on the right side. Mayer [5] reported a case of a 64 year old man who had visual hallucinations and did not admit his blindness. Bilateral softenings of the medial surfaces of the occipital lobes were found. Lunz [6] described a case of complete blindness in which the fundi and pupils were normal; the patient was not aware of his defect. Bilateral occipital softenings were found. Bonhoeffer [7] described a patient with alexia who was not aware of his inability to read. Lejoune, Raymond and Galezowski [8] reported the case of a 57 year old man with pseudobulbar palsy; the patient recovered from the first attack of blindness, which he noted, but was unaware of his second attack; autopsy was not performed. Probst [9] reported the case of a 62 year old man who had a cerebral accident followed by hemianopsia at the age of 56, became aphasic and confused at 57 and had right hemiplegia, dysarthria and cortical blindness at 58. He remained indifferent toward his blindness and thought that he was in a dark cellar most of the time. An extensive, butterfly-shaped glioma filling large parts of both hemispheres and softening of both occipital lobes were found.

In 1908 E. Redlich and Bonvicini [10] published careful observations on 3 patients with Anton's syndrome. The case of a fourth was published in a subsequent paper. The first patient, a 21 year old man, was admitted with epileptic attacks and headaches. He was temporarily confused, disoriented and euphoric. He had defects of memory and retention but was not grossly deteriorated. He had no aphasia or apraxia. He was totally blind; his pupils did not react to light, and the disks were choked. He was absolutely unaware of his blindness; he thought his vision was intact. A tumor in the region of the septum pellucidum involving both sides of the centrum semiovale and the heads of both caudate nuclei was found. No pathologic diagnosis was made. The second case was that of a 49 year old woman who had right hemiparesis and mild aphasic disturbances and within eight months became totally blind. Neurologic examination revealed bilateral optic neuritis. The pupils were wide and did not react to light. There was slight right hemiparesis, and the deep tendon reflexes were more active on the right side than on the left. The Babinski sign was present bilaterally. There was slight amnestic aphasia and no apraxia; tactile recognition was normal. The patient was forgetful of events of the recent past; she was disoriented for date and place but did not show any gross deterioration. She confabulated about her vision, though she was totally blind; usually she said it was dark, and she used all kinds of alibis if she failed to identify objects correctly. Her recall of colors and forms from memory was good. She usually populated her environment with various persons from earlier life. Autopsy revealed an endothelioma the size of an egg which arose from the clivus and compressed half of the pons and the cerebellum. The third, seventh and eighth nerves on the left side showed compression atrophy; there were secondary optic nerve atrophy and internal hydrocephalus. The third case was that of a 72 year old janitor who was admitted to the psychiatric clinic. Nine months before his admission headaches and left homonymous hemianopsia developed. Five days before his admission right hemianopsia developed, and he became totally blind. He complained about darkness, asked "for light," was unable to identify

3. Dejerine and Vialet: Sur un cas de cécité corticale, Compt. rend. Soc. de biol. **11**:983-997, 1893.

4. Rossolimo, G.: Ueber Hemianopsie und einseitige Ophthalmoplegie vasculären Ursprungs, Neurol. Centralbl. **15**:626-637, 1896.

5. Mayer, C.: Eine doppelseitige homonyme Hemianopie mit Orientierungstörungen, Monatschr. f. Psychiat. u. Neurol. **8**:440-462, 1900.

6. Lunz, C.: Zwei Fälle von korticaler Seelenblindheit, Deutsche med. Wchnschr. **1**:381-393, 1897.

7. Bonhoeffer, K.: Casuistische Beiträge zur Aphasielehre, Arch. f. Psychiat. **37**:564-597, 1903.

8. Lejoune, Raymond and Galezowski: Cécité corticale par double hemianopie, Rev. neurol. **19**:680-691, 1906.

9. Probst: Ueber einen Fall vollständiger Rindenblindheit und vollständiger Amnesie, Monatschr. f. Psychiat. u. Neurol. **9**:5-21, 1901.

10. Redlich, E., and Bonvicini, G.: Weitere klinisiche und anatomische Mitteilungen über das Fehlen der Wahrnehmung der eigenen Blindheit bei Hirnkrankheiten, Neurol. Centralbl. **30**: 227 and 301, 1911; Ueber das Fehlen der Wahrnehmung der eigenen Blindheit bei Hirnkrankheiten, Jahrb. f. Psychiat. **29**: 1-134, 1908.

objects and recognized people only by their voices. He never admitted his blindness. The patient exhibited no aphasic difficulties but had pronounced dysgraphia. He showed mild deterioration and had slight defects of memory for remote and recent events; he was able to repeat only four digits. His optic recall for numbers and forms was normal. Neurologic examination revealed slight spastic hemiparesis and hemihypesthesia on the right side. The pupils and fundi were normal. The patient died, and the autopsy revealed thrombosis of both occipital arteries and extensive softenings of the mesial and basal parts of the occipital lobes. The uncus, hippocampus, visual radiations and fornix showed extensive softenings.

The fourth case was that of a 64 year old man who was admitted with weakness of the right arm and right hemianopsia after a cerebral accident. In a second accident the patient became totally blind. He was not aware of this blindness and did not admit it at any time. He confabulated constantly and showed slight impairment of intelligence. He was rather attentive, but his memory for recent and remote events and his retention were very poor. His spatial orientation was badly impaired.

Redlich and Bonvicini drew attention to the fact that the syndrome is not rare; in most cases observed there is bilateral hemianopsia. In the majority of cases there are lesions of the occipital lobe, but the syndrome occurs in cases of generalized disease of the brain with blindness. Deterioration alone does not explain the syndrome.

Albrecht,[11] Anton's pupil, described 3 cases. In the first, a 53 year old colonel had slowly progressing spastic hemiplegia on the right side. He had bilateral papilledema and was completely blind. His pupils were fixed to light. He always complained of darkness but never admitted to being blind. At first he showed only slight intellectual deterioration. Later on he became confused and hallucinated. Autopsy revealed hypernephroma of the right kidney and a metastatic lesion, the size of an egg, in the left parietal region and another in the cerebellum. The second case was that of a 41 year old laborer who was admitted with complaints of headache, dizziness, lack of critical ability and difficulties in the naming of objects. Both disks were choked, and the patient had left hemiplegia, left analgesia and astereognosis. Four months later he became comatose and was completely blind when he recovered from the episode. He thought, however, that he was able to see. Autopsy showed a sarcoma of the posterior part of the right thalamus, extending into the lateral ventricle. The third case was that of a 31 year old business man who had headaches, right hemiparesis and complete blindness. He was hypomanic and euphoric; at times he had delusions of persecution and became rapidly confused. He was rather deteriorated and showed considerable impairment of memory. He had atrophy of both optic nerves and spastic hemiparesis of the right extremities. He believed that everything was dark, used constant subterfuges in regard to his lacking eyesight and stated that he could see perfectly well. Autopsy revealed a tumor of the left frontal lobe, the size of a man's fist. Albrecht maintained Anton's theory that the syndrome is due to an interruption of neural conduction between remote cortical areas in different lobes. When association tracts are interrupted, the lack of sensory stimulation due to blindness or deafness is no longer perceived.

Poetzl[12] described disturbances of perception in cases of left hemiplegia and discussed the lack of perception of blindness. He stressed the frequency of the syndrome, particularly among patients with dementia paralytica with optic nerve atrophy. He was the first one to emphasize that the syndrome of anosognosia, a term coined by Babinski,[13] may be due to two lesions, one in the thalamus and the other in the parietal cortex, or to one subcortical parietal lesion. Tunero[14] described a patient with a tumor in the right pulvinar the size of a goose egg who presented Anton's syndrome. Weber[15] described the case of a patient with two consecutive cerebral accidents in the course of bacterial endocarditis; the second accident was followed by blindness, which he denied. Raney and Nielsen[16] reported briefly 2 cases of denial of blindness. The first was that of a 47 year old man with complete loss of vision, left hemiplegia and left homonymous hemianopsia. The patient claimed he could see objects on both sides, although he named objects incorrectly on the left side. The

11. Albrecht, O.: Drei Fälle mit Antons Symptom, Arch. f. Psychiat. **59**:883-941, 1918.

12. Poetzl, O.: Ueber Störungen der Selbstwahrnehmung bei linkseitiger Hemiplegie, Ztschr. f. d. ges. Neurol. u. Psychiat. **93**: 117-168, 1924.

13. Babinski, M. J.: Contribution à l'étude des troubles mentaux dans l'hémiplégie organique cérébrale (anosognosie), Rev. neurol. **27**:845-848, 1914.

14. Tunero, J.: Ein Fall mit Antons Symptom, Psychiat. et neurol. japon. **41**:679-690, 1931.

15. Weber, F. P.: Agnosia of Hemiplegia and of Blindness After Cerebral Embolism, Lancet **1**:44-46, 1942.

16. Raney, A. A., and Nielsen, J. M.: Denial of Blindness (Anton's Symptom), Bull. Los Angeles Neurol. Soc. **7**: 150-151, 1942.

other case was that of a 54 year old woman who was completely blind; she could not distinguish daylight from darkness but described objects. No autopsy was done.

REPORT OF PRESENT CASES

CASE 1.—M. T., a 49 year old white American housewife, was admitted to the New Haven Hospital on July 9, 1943. Four years before her admission the patient first noted double vision, which disappeared when she changed her glasses. In the spring of 1943 she again noted a decrease in vision; particularly, she felt unable to see from side to side as well as formerly. She began to have headaches, chiefly in the parietal and occipital regions, which were intermittent, rather severe and occurred mostly in the morning. There was also roaring in the left ear. She vomited a few times, without any nausea, and had several attacks of numbness over the right side of her face, which lasted about a minute. The patient complained of some loss of memory for recent events in the months before her admission. The past medical history was not contributory. She came of lower middle class Yankee stock, went through grammar school as far as the eighth grade, had been married for twenty-five years and had twelve children, ranging from 24 to 3 years of age. She worked at home and was apparently well adjusted and contented. There was no history of any severe psychologic problems or of alcoholism. The family history was not contributory.

Physical examination showed obesity and a blood pressure of 170 systolic and 110 diastolic; there were no signs of cardiac decompensation. The pulse rate was 84 and the temperature 98.6 F. Vision was greatly diminished, so that she was unable to read even the largest newspaper print. Examination of the visual fields showed left lower quadrantanopsia. There was bilateral papilledema, of 4 D. The pupils were about 6 mm. in diameter; they were round and regular, did not respond to light but reacted in convergence. There were no objective findings pertaining to the fifth nerve. Hearing was not impaired objectively. The cranial nerves were otherwise normal The left palpebral fissure was narrower than the right.

Strength, coordination and muscular tone of the trunk and the extremities were normal. The sensory status was normal. The abdominal reflexes were present on both sides. All deep tendon reflexes were hyperactive and equal on the two sides. The plantar responses were diminished.

Laboratory Data.—The urine was normal. The Kahn reaction of the blood was negative. The blood count showed 20 Gm. of hemoglobin per hundred cubic centimeters, 4,140,000 red cells, 5,400 white cells and a normal differential count. The nonprotein nitrogen measured 33 mg. per hundred cubic centimeters. An electroencephalogram was normal. A roentgenogram of the skull revealed increased convolutional atrophy and enlargement and erosion of the sella turcica, probably secondary to increased intracranial pressure. The diagnostic impression was tumor of the brain stem or of the hypothalamus.

Ventriculographic examination, on July 15, pointed to a midline tumor of the midbrain, resulting in elevation of the floor of the third ventricle, with a complete block at the origin of the aqueduct of Sylvius and obstructive hydrocephalus. The roentgenologist thought that the tumor might be a pinealoma. On July 26 a craniotomy in the right parietal area was performed by one of us (J. F. D.), the splenium of the corpus callosum split and the third ventricle entered, but no tumor could be found in the region of the pineal gland, the hypothalamus or the midbrain. The patient's immediate postoperative course was uneventful. However, on August 9 she became confused and agitated; she was completely disoriented and was euphoric; she seemed to hear voices of persons she knew, saw members of her family, though they were not present, and talked at random. It appeared at that time that the patient was completely blind but seemed to disregard her blindness. When asked how many persons were present in her room, she would guess wrong, and she gave completely false descriptions of persons and objects in her room and of the examiner. When a light was flashed directly in front of her eyes, she was unable to say when the light was on or off. When her blindness was pointed out to her, she would reply, "Oh. I see all right. It's quite dark, but I see you." There was evidence of intellectual deterioration. The patient was only roughly oriented for current events and showed but little knowledge of topics of common interest, such as the war, prices and rationing. She was unable to define differences between a river and a lake or a midget and a child, or to make statements about similarities of an orange and a banana or a buggy and an automobile. She would not cooperate even in the simplest calculation. There was evidence of an amnestic aphasia. She seemed to have severe defects in her memory of recent events and could not remember that she had been operated on. She was unable to retain the examiner's name, even for three minutes. She did not know that she was in the hospital and thought she was at home. There was no astereognosis. On August 30 a suboccipital craniotomy (by Dr. Bernard Brody) was carried out and no tumor was found. The immediate postoperative course again was good, but gradually the patient showed advanced deterioration. She lay motionless in her bed, would not talk, became incontinent and had to be fed. The neurologic signs did not change materially except that secondary optic nerve atrophy developed. The patient remained in the hospital in a vegetating condition until Jan. 8, 1944, when she was taken home for economic reasons.

The diagnosis remained unclear; the presence of a hypothalamic tumor was unverified, and the question of an obstruction of the sylvian aqueduct, of unknown cause, arose.

CASE 2.—J. C., an 8 year old white boy, was admitted to the New Haven Hospital on Oct. 2, 1943, with the complaint of blindness.

Four years before his admission he had an acute attack of otitis media of the left ear; thereafter the ear drained intermittently. In August 1943 his tonsils and adenoids were removed, and shortly afterward "boils" developed in the canal of the left ear. During the first week of September he complained of pain in the left eye, the left shoulder and the left side of the neck. At this time he was given "vitamin B_1 for toxic neuritis." Fifteen days before admission to the hospital he "went blind." Three days later he had a stiff neck and was treated for meningitis at another hospital. Nine days before his admission a mastoidectomy was done on the left side. Cultures showed Staphylococcus albus. After the operation he was given a transfusion and appeared to be doing well until the day before his admission, when he began to vomit. Examination of his eyegrounds showed papilledema. He was referred to this hospital for admission.

The family and the past history were noncontributory.

Physical Examination.—The boy was pale and appeared chronically ill; he was alert and talkative.

There was a bandage over the left ear. The right pupil measured 4 mm. and the left 3.5 mm. The right pupil did not react to light. The left pupil showed minimal contraction to light, and light shined into this eye caused consensual contraction of the right pupil. He was unable to see light when a flashlight was shined directly into the right eye. On the left side he could recognize light only in the temporal field. The fundi showed choking of the disks, measuring 4 D.; the vessels were extremely tortuous. There was inability to turn the left eye to the left beyond the midline or to turn that eye down and out. Otherwise the cranial nerves were intact. The neck was rather stiff. The extremities were equally strong on the two sides. Motor coordination was good. Sensations for touch, pinprick and position were intact. All deep reflexes were absent; the plantar response was diminished on the right side and equivocal on the left. Numbers written in his hands were recognized. When he was given objects to name, he called a safety pin a "big pen" or a "straight pen." Calculations were poorly done; $2 \times 3 = 7$ and $4 \times 3 = 7$. When asked to multiply 6 by 9 and to add 9 and 14, he replied, "Can't do." When he was asked to touch his left hand to his right shoulder, he put his left hand on his right elbow. When asked to touch his right hand to his right ear, he touched his left hand to his right ear. When given a pen and asked to write, he wrote his name and address and wrote to simple dictation. He could feed himself with a fork and a spoon. The clinical impression was that of an abscess of the superior part of the left temporal lobe.

On Oct. 4, 1943, during a ventriculographic study, the wall of an abscess was encountered 3 cm. below the burr hole in the left occipital area. The left ventricle could not be tapped. The right ventricle and the third ventricle were shifted to the right. Operation was performed on the same day by one of us, J. F. D. An incision was made anterior to the left ear; after removal of some of the bone, the dura was opened, and the wall of an abscess was encountered at a depth of 0.75 cm. Fifty cubic centimeters of thick, yellow, putrid pus welled forth. A second, large, connecting cavity was found posteriorly. Iodized poppyseed oil was instilled into the depths of the cavity, which was then packed with petrolatum gauze after a Penrose drain had been inserted.

Postoperative roentgenograms showed the iodized oil to be "approximately 3 cm. from the inner table of the temporal bone in the frontal view, while in the lateral view it appeared to be above the tip of the mastoid." On the day after the operation the pupils no longer reacted to light or consensually. Moreover, when a flashlight was shined directly into either eye, the patient was unable to tell whether the light was on or off. At this time he maintained that his vision was good; he described his physician as wearing a hat, although actually none was worn. He made similar mistakes in other tests. When asked to point to the window or the door, he would point in various directions. When his errors were explained to him, he still would not admit that he was blind. When asked whether he could see, he said he could see well. When he was told to look at objects and to name them, he made wrong guesses. When his mistakes were pointed out to him, he did not seem surprised and insisted that his eyesight was good. When told directly that he could not see, he again retorted that he could see well. This behavior persisted two more days. On October 8, when his vision was tested with a flashlight, he could not tell whether the light was on or off; and when he was asked whether he was not blind, he said "I don't care if I can't see." To most questions involving vision he replied "I don't know."

On October 11 he could tell for the first time when a light was shined onto either the nasal or the temporal field of the left eye. There still was no pupillary response to light. A small fungus developed in the wound, but by October 30 the fungus was pulsating. On November 28 the right eye was blind. The left pupil measured 4 mm., the same as the right; the left pupil reacted to light and the right consensually. The patient still had trouble in remembering the sequence of the months and the correct order of words in his prayers. He was unable to state when Christmas is, nor did he know how many weeks or days there are in a month. Calculations were done as before: $4 \times 3 = 7$, and $4 \times 2 = 6$. He identified objects placed in either hand. The wound in the head was completely healed by December 5, and he was discharged on that date. Thereafter he continued to do well; and when he was seen on January 11, vision had improved so that he was able to count fingers at 3 inches (7.6 cm.) with his left eye and was aware of the blindness of the right eye. He still omitted four months when asked to name the months of the year in order. He did calculations correctly: $7 + 5 = 12$; $4 \times 3 = 12$; $6 \times 4 = 24$; $15 - 7 = 8$. He readily obeyed complicated commands pertaining to the body scheme.

CASE 3.—A. J., a white man aged 46, a machinist, was admitted to the New Haven Hospital on Oct. 3, 1943, complaining of blurred vision in his right eye of three weeks' duration.

Present Illness.—Three and a half weeks before entry to the hospital, while working, he felt a sharp pain in the right eye and thought that a particle had got into the eye. There was no redness or watering, and the pain subsided in about a half-hour, to recur intermittently thereafter. Three days later, while inspecting a finished product with a magnifying ocular, he noted that he could see nothing with the right eye. When he closed the left eye, he realized that the right eye was completely blind except for "hazy vision" in the upper field. He could not see objects directly ahead or below him. He also noted sharp pain on movement of the eye to either side and a sense of pressure behind the eye. About the same time there were intermittent "sharp pains deep in the bones" of the right cheek and temple and the right side of the forehead. These lasted from a few minutes to two or three hours and usually were relieved by acetylsalicylic acid.

One week before his entry there was blurring of vision in the left eye, which increased in intensity so that on admission he was able to read only headline type in the newspapers. For three days prior to admission he had had a chest cold.

The family and the past medical history were not contributory.

Physical Examination.—The patient was well developed, stocky and slightly obese. He did not appear to be in distress. General physical examination revealed nothing remarkable. The temperature was 98.6 F., the blood pressure 128 systolic and 104 diastolic, the pulse rate 76 and the respiratory rate 12 a minute. The head was symmetric. There was hyperesthesia to light touch, but not to pain or to deep pressure, over the cheek, the periorbital region, the forehead, the temple and the parietal region on the right side. The right pupil was 4 mm. and the left 3 mm. in diameter. The right pupil reacted sluggishly to light; the left, promptly. Extraocular movements were full; there was no nystagmus. There was pronounced concentric constriction of the visual field of the left eye. Determination of the field

of the right eye was not possible. There was bilateral choking of the disks, measuring 3 D. In the upper third of the left disk was a small perivascular area of brown-red pigmentation, which appeared to be an old hemorrhage. Otherwise the cranial nerves were normal. Muscular strength was good in all extremities. The knee and ankle jerks were livelier on the right side than on the left. Associated movements on walking were more noticeable on the left side than on the right. The finger to nose test was not as well done on the right side as on the left.

Laboratory Data.—The blood count showed 4,800,000 red cells, hemoglobin 88 per cent and 9,600 white cells. The Kahn reaction of the blood was negative. Urinalysis revealed a specific gravity of 1.007, no albumin and no sugar. Microscopic examination showed no cells or casts. Roentgenograms of the skull revealed the right optic foramen to be slightly larger than the left. The cortical outline was thinner on the right side. Lumbar puncture revealed an initial pressure of 350 mm.; after 12 cc. of clear, colorless spinal fluid was withdrawn, the final pressure was 180 mm. The fluid contained 28 lymphocytes and 8 polymorphonuclear cells per cubic millimeter; the total protein was 510 mg. per hundred cubic centimeters. The Wassermann reaction of the spinal fluid was negative, and the colloidal gold curve was 0000000000.

Three days later there was slight flattening of the nasolabial fold on the left.. The corneal reflexes were now absent bilaterally. A ventriculogram was made on October 16. The ventricular fluid did not appear to be under tension, and 40 cc. of fluid was removed. However, the filling was unsatisfactory. The roentgenograms showed subdural air over the right hemisphere and slight dilatation of the anterior horns.

After ventriculographic examination there was rapid reduction of the remaining vision in the right eye, so that determination of the visual fields on October 21 showed complete loss of vision of the right eye and visual acuity of 6/100 in the left eye, with some constriction of the upper temporal field in the left eye. Five days later there was further constriction of the superior and temporal fields in the left eye, vision in that eye now being 1/40—2. Since the ventriculograms failed to show any evidence of an expanding lesion, the patient was discharged from the hospital on November 3. He was readmitted on November 17 because during the two weeks he had been away there had been complete loss of vision in the left eye, and he was now completely blind. He had also noticed "dizziness" on standing or sitting up quickly. Physical examination showed that the pupils were small, measuring 2 mm., and did not react to light; the disks were about the same as before, and, while the extraocular movements were still full, there was now fine sustained nystagmus on extreme lateral gaze to the right or to the left. Two days later the nystagmus was more pronounced to the right. The right disk was whiter than the left; both were swollen, the left more than the right. On November 24 a pneumoencephalogram was made. Again, there was poor filling, and the films were of no diagnostic value. Ventriculographic examination was repeated on November 26, and this time irregularity of the wall and the floor of the right anterior horn was seen. There was incomplete filling of the anterior portion of the third ventricle. An electroencephalogram taken on December 2 showed a focus of slow waves in the right frontotemporal area.

After the second ventriculographic examination the patient began to have intermittent elevation of temperature, sometimes reaching 101 F. He was disoriented for time and place. He said that he could see; but when he was asked whether a light was shined in his eyes, he made numerous errors and could not point out the position of the light. He described the suit that the physician wore, calling it brown, when actually it was white. He could not point to either the window or the door of his room. The patient was obviously blind but did not seem to notice this himself. When it was explained to him, he refused to believe it. He attempted to reach for objects, and when given them, tried to handle them as though he could see. At times he had difficulty in naming the objects he handled.

By December 10 the patient responded only in mumbles, appeared stuporous, refused to eat and had to be fed with a tube. He preferred to lie with his head and eyes turned to the right, and forcible turning of the head to the left caused him to moan with pain. The neck was stiff; Kernig's sign was present bilaterally, and the plantar response was equivocal on the left and diminished on the right. The next day he was comatose. On December 12 the temperature, which had gone progressively higher on the three preceding days, reached 105 F. The pulse rate was 120 and the respiratory rate 60. He was cyanotic; the distal extremities were cold, and he died the same day.

Anatomic Study (Dr. Hildegard Arnold).—There was a small cerebellar pressure cone. The right optic nerve was thickened by an inherent tumor, so that the nerve appeared to be about three times its normal diameter. The tumor involved the entire floor of the third ventricle and was adherent to it. The pituitary body was normal. There was a firm, slightly hemorrhagic mass filling the whole of the third ventricle and replacing most of the hypothalamic structures. The growth had extended in plaques to involve the orbital gyri of both frontal lobes.

Anatomic Diagnosis.—The diagnosis was primary sarcoma involving the optic chiasm and the tuber cinereum, with flattening of cerebral gyri.

CASE 4.—J. C., a Russian Jew aged 62, was admitted to the psychiatric clinic on April 19, 1944, with symptoms of anxiety, depression and agitation, after several abortive attempts at suicide. In the summer of 1943 the patient, after some domestic worries, became run down. She lost weight, could not sleep and complained of constant burning in her stomach. A diagnosis of "leukemia" was made, and the patient was treated with liver and pentnucleotide until the blood picture became normal again. Two weeks before admission she became tense, agitated and anxious, slashed her wrist and swallowed a piece of wood. She moaned and complained constantly and was admitted to the psychiatric clinic.

Her medical history was not contributory. The menopause occurred at the age of 52. The patient had six children, all of them highstrung but physically well. She had been born in Russia and had come to the United States at the age of 17 years. She had been a fairly well adjusted, outgoing, hard working, aggressive woman, who held the family together and had been responsible for its social rise.

Physical Examination.—The physical status was normal except for hypertension, with a pressure of 170 systolic and 98 diastolic, slight enlargement of the heart, accentuation of the aortic second sound and a soft, blowing apical and pulmonic diastolic murmur. The electrocardiogram showed an axis shift characteristic of hypertrophy of the left ventricle. The rest of the physical examination and all laboratory tests (a Kahn test of the serum, studies of the blood and urine, roentgenographic examination of the skull, serial roentgenographic study of the gastrointestinal tract, pyelographic examina-

tion, lumbar puncture, electroencephalographic studies and examination of the stools) gave normal results. Excretion of the dye in the phenolsulfonphthalein test was normal. The nonprotein nitrogen measured 34 mg. per hundred cubic centimeters. The patient continued to be anxious, agitated and depressed; she thought that she was incurably sick and complained constantly of "burning up." Otherwise there were no delusions or hallucinations. There was no evidence of deterioration. The sensorium was clear, and memory and retention were normal.

Treatment consisted of administration of large doses of barbiturates by day and use of paraldehyde and wet packs at night. On April 26, at 8:30 p. m., she complained about dizziness and said she had fallen. Examination at that time revealed nothing significant. At 9:30 p. m. the patient was discovered lying across the bed in an attitude of prostration, with cold, clammy, blue skin and stertorous breathing; the pulse was good, and the blood pressure was 110 systolic and 70 diastolic. The patient was comatose for about half an hour. Neurologic examination revealed nothing significant. When she regained consciousness, she was confused and disoriented and had considerable difficulty in understanding and expressing herself. On the morning following the attack it was noted that the patient did not recognize any objects. She could not say correctly where the door or the windows were, nor how many persons were in the room. She was unable to see strong light in front of her eyes. She made false descriptions of the appearance of persons in the room. It was evident that she was blind and did not perceive her blindness. When asked whether she was blind, she denied it. Her pupils were 5 mm. in diameter; they were equal and regular and reacted to light. Neurologic examination revealed no abnormality except for absence of the abdominal reflexes and a bilateral Babinski response. The retinal vessels appeared extraordinarily thin. During the examination the patient had a second attack, which was almost identical with the one on the previous evening except that it was more severe and of longer duration. She was comatose for about two hours and then gradually recovered consciousness. In this state she had definite jargon aphasia with inability to comprehend. On the following day the aphasia and all pathologic and neurologic signs, including the blindness, has disappeared. The patient seemed much improved mentally and was calm, friendly and cooperative. There were no hypochondriacal complaints. The retinal vessels showed slight arteriosclerosis but were not as thin as during the attack. The patient was oriented; her memory seemed good except for complete amnesia for her attacks. It was as though she had "shocked" herself out of her agitated depression. The nature of these attacks remained unclear. Possibly she had cerebral angiospasm which caused temporary focal symptoms, aphasia and blindness, with Anton's syndrome. One week after the attack the patient was just as psychotic as before and remained so until her discharge to another hospital, on June 20, 1944.

Case 5.—C. C., a 59 year old woman, was admitted to the New Haven Hospital for the second time on July 3, 1944. Known to be diabetic since 1932, she responded to diet therapy, and use of insulin was unnecessary until 1939. In 1936 she noted deterioration of vision in both eyes, particularly the left. An ophthalmologist found hemorrhages in both retinas. In 1940 vision in her right eye became temporarily worse, and for a short while she was unable to see at all. Her vision improved again for several months and then became gradually poorer. On Sept. 25, 1941 the patient was admitted to the New Haven Hospital for the first time, on account of rapidly failing vision.

Physical examination revealed a blood pressure of 225 systolic and 84 diastolic; otherwise the vital signs were normal. The fundi were obscured by opacities, presumably in the lens. The heart was slightly enlarged to the left. The patient had 4 plus pitting edema of both legs. There is no report of any personality disturbance, and the results of neurologic examination were normal.

Laboratory Data.—The urine gave a 4 plus reaction for albumin and contained sugar. The blood count revealed 3,000,000 red cells, 71 per cent hemoglobin, 5,700 white cells and a normal differential count. The Kahn reaction of the blood was negative. The nonprotein nitrogen of the blood measured 29 mg. per hundred cubic centimeters. The fasting blood sugar level was 149 mg. per hundred cubic centimeters; the serum protein measured 5.56 Gm. per hundred cubic centimeters; the phenolsulfonphthalein test showed excretion of only 11 per cent of the injected dye in four hours. A roentgenogram of the chest showed enlargement of the left ventricle; there was hypertrophic osteoarthritis and calcification in the left upper quadrant of the abdomen, of undetermined cause.

A diagnosis of intercapillary glomerulosclerosis (Newburger and Peters,[17] Kimmelstiel and Wilson[18]) was made. The patient was followed in the metabolism clinic, and treatment with a high protein, antidiabetic diet and small doses of insulin was continued. Under this regimen she was able to hold her own until the spring of 1943, when her eyesight began to fail notably. The nonprotein nitrogen had risen to 52 mg. per hundred cubic centimeters, and an ophthalmologist found numerous punctate opacities in the vitreous and retinal hemorrhages. In the summer of 1943 she was unable to work as supervisor of a boys' camp because of poor vision. On May 10, 1944 it was noted that she was "wandering mentally." At the time of her second admission the physical findings were as follows: The vital signs were normal. The blood pressure was 220 systolic and 110 diastolic. There had been no changes with respect to the heart since her first admission except that she had no edema. For all practical purposes the patient was blind. She had to be fed and taken care of like a blind person. She flinched away from a strong light directly in front of her eyes but was unable to localize the light. The right pupil measured 4 mm. and the left 3 mm.; both reacted promptly but minimally to light. The bulbi seemed tender, and the patient resented examination of the eyes. The ophthalmologist, Dr. E. Blake, saw many large, stringy opacities in the vitreous body of each eye. The retinal vessels were sclerotic, and there were retinal hemorrhages in the right eye. The left fundus could not be seen clearly. The other cranial nerves and the motor system were intact. The patient felt pinprick all over her body; evaluation of her sense of touch, vibration and position was impossible. All the deep reflexes were present and physiologically active except for the absence of ankle jerks. The Babinski sign was present on the left side. Urinary incontinence was noted occasionally.

Laboratory Examinations.—The blood count showed 3.400,000 red cells, 12.5 Gm. of hemoglobin per hundred

17. Newburger, R. A., and Peters, J. P.: Intracapillary Glomerulosclerosis: A Syndrome of Diabetes, Hypertension and Albuminuria, Arch. Int. Med. **64**: 1252-1264 (Dec.) 1939.

18. Kimmelstiel, H., and Wilson, C.: Intracapillary Lesions in the Glomeruli of the Kidney, Am. J. Path. **12**:83-98, 1936.

cubic centimeters, 9,500 white cells and a normal differential count. The Kahn reaction of the blood was negative. The urine gave 4 plus reactions for albumin and sugar (on admission). The cerebrospinal fluid was under an initial pressure of 200 mm. of water. The total protein content was 51 mg. per hundred cubic centimeters; there were no cells; the colloidal gold curve was 0000000000.

The patient was quiet and cooperated to the best of her ability. She was talkative and answered all questions, though she did not understand the more complex questions. There was no aphasia. She was completely disoriented and thought she was in a religious school. She stated that it was December, though the weather was warm, and said that the year was 1918, 1940 or 1945. Her retention and memory for recent events were highly defective. She had hardly any information about the war except that she knew that the country is at war. She was unable to give her address but could give her name and her husband's name. Her knowledge of the remote past was better. Speech was incoherent and irrelevant and at times almost rambling, with a marked flight of ideas. She seemed rather euphoric and had no idea that she was either mentally or physically ill. Although she was almost amaurotic, she acted and spoke as though she could see well. She described the room, the places of doors and windows and the number, names and appearance of persons, but her statements were false. She was unable to state whether a light in front of her eyes was on. At all times she localized such a light inaccurately. In her confabulations she made detailed but false statements about the occurrences in the room. When asked whether she was blind or did not see well, she made vigorous denials. When told she was blind, she did not acknowledge it. On July 12, 1944 the patient had a cerebral accident without loss of consciousness; left hemiparesis, involving the face and the extremities, was noted. She was unable to move the extremities spontaneously; muscular tone was decreased. The patient reacted to pinprick by withdrawal of the left leg and slight movements of the left arm. No other sensory examination could be carried out. The deep reflexes were slightly more active on the right side than on the left. There were dorsiflexion and withdrawal to plantar stimulation on the left side and plantar flexion on the right. The patient was unaware of her left hemiparesis and even denied its presence when it was pointed out to her. However, she was aware of the existence of her left extremities. Subsequent examinations showed no changes up to the time of her discharge, on Aug. 4, 1944.

CASE 6.—P. K., a white man aged 45, was admitted to the New Haven Hospital for the first time on March 25, 1942. One week before admission he complained of severe frontal headaches and dizziness and became slightly confused. He reported seeing yellow lights on his left side. The past personal history was not contributory. The patient was of Irish-American stock, born and raised in Connecticut; he graduated from high school. For thirteen years he had been a widower. He was a successful manager of a small mattress factory. He had always been a stable, pleasant, outgoing person and had shown no peculiarities or maladjustment in his behavior. There was no indication of any psychopathic trends.

The physical examination gave normal results except for the neuropsychiatric changes to be described. The patient was pleasant, cooperative, conscious and oriented. There was no evidence of intellectual deterioration. Motor speech and comprehension were normal except for occasional difficulties in naming objects. There were noticeable dyslexia and dysgraphia. Right homonymous hemianopsia was present. The fundi showed bilateral papilledema, of 3 D. The pupils were normal. The other cranial nerves and the motor and sensory systems were intact. The reflexes were physiologic. A roentgenogram of the head showed an "asymmetric skull, convolutional atrophy and displacement of the pineal gland to the right." An electroencephalogram revealed "a focus of slow waves in the left temporal lobe." The diagnostic impression was that of a cerebral neoplasm in the left parieto-occipital region. On April 1, 1942, ventriculographic examination and subequent craniotomy were carried out (Dr. W. Klemperer). A soft, fleshy, reddish tumor was found in the subcortical portion of the inferior parietal and posterior temporal region on the left side, extending toward the occipital lobe. A specimen, measuring 6 by 4 by 5 cm., was removed. The histologic diagnosis (Dr. H. Zimmermann) was glioblastoma multiforme.

The patient recovered rapidly; lost his aphasia, dysgraphia, dyslexia and hemianopsia, and was asymptomatic from May to November 1942. In November 1942 he reported two incidents of glassy vision. On Dec. 7, 1942 he had one attack of complete disorientation while driving a car. In January 1943 he experienced three attacks of complete blindness, each lasting several hours. At that time his symptoms of amnestic aphasia reappeared. His memory was impaired. He was unable to write and could barely detect movements of a hand in front of his eyes. The disks showed bilateral choking, of 3 D. On Feb. 11, 1943 a ventriculographic examination and craniotomy on the right side were carried out (Dr. William T. German). It was observed that the tumor had spread through the posterior part of the corpus callosum; a 2.5 cm. specimen of solid tumor was removed by suction from the right occipitoparietal region. The postoperative course was uneventful but the neurologic signs remained unchanged. At that time it was noted that he pretended to see, though he was obviously blind.

On March 19, 1943 the patient was transferred to the psychiatric clinic. He was moderately restless but cooperative, although he finally had to be helped in eating and with care of his body. He knew he was in the New Haven Hospital, but he was unable to remember the operation unless he was reminded of it. Memory for the remote past was fair. He showed pronounced amnestic aphasia and agraphia. He was paranoid toward his family and persistently demanded to be discharged. On all clinical examinations he was completely unable to distinguish strong lights from darkness. The only examination which revealed a trace of vision was the psychogalvanic skin test, carried out by Prof. Donald Marquis. Both disks showed signs of secondary atrophy. The pupils were about 6 mm. in diameter and were equal, round and regular; they reacted promptly and extensively to light and in convergence. The cranial nerves were intact. Muscular strength and tone of the extremities were physiologic. There were bilateral action tremor and past pointing in the finger to nose test and slight ataxia in the heel to shin test. Position sense and vibration sense of the trunk and the extremities were definitely impaired. Touch, temperature and pain senses, topognosis and two point discrimination were normal, as was body perception. There was no finger agnosia. Recognition of materials was good, but recognition of forms was impaired beyond that due to his amnestic difficulty. All deep tendon reflexes were normal. The abdominal and cremasteric reflexes were absent; the plantar reflexes were of flexor type.

His ability to cooperate in formal testing procedures (Dr. Margaret Keller) was extremely limited, owing to his distractability, confusion and aphasia. He showed difficulty in comprehension, which was greater at some

times than at others. In the Binet vocabulary test, which under such circumstances was not very valid, the patient succeeded in defining the average number of words for adults. This was, however, not achieved under standard conditions. Words were repeated for him when necessary, and he was given several trials unless his response indicated that he did not know the word to be defined. On the verbal half of the Wechsler-Bellevue test his performance was extremely inferior. He could answer a few of the questions relating to general information and comprehension but succeeded with only one problem in arithmetic and failed completely in the similarity test, being unable to grasp what was required of him. He showed a notable deficiency in all tests involving memory, repeating only three digits forward and two in reverse with many repetitions and instructions. He could remember only one item from a paragraph immediately after it had been read to him. He frequently forgot the question asked before he was able to complete his answer. It was noticed that his memory improved when distractions were reduced to a minimum during the period of delay preceding recall. The patient showed perseverative tendencies at times. He seemed to become fixed on a certain type of response and to be unable to change unless distracted by some irrelevant stimulus. The total impression received was that of extreme intellectual deterioration.

At all times when he was asked, the patient said that he was able to see. He moved about in his room as though he could see and constantly bumped into objects. When this was pointed out to him, he used excuses such as: "It is a little dark"; "This is not a bright day," and "I'm tired." When asked directly whether he was blind, he vigorously denied it, though at times he would say "I don't see as well as I did before, but I can see all right. I need new glasses." He made constant false guesses about the location of windows and doors and the appearance of persons in his environment. His memory for forms and colors was correct. The syndrome of denial of blindness remained constant as long as a psychologic examination was possible, which was approximately until the first week of June 1942.

The patient became steadily worse; both cranial flaps showed considerable ballottement, which gave his head a grotesque appearance. In May and June 1942 he had episodes of severe excitement, often yelling at the top of his voice, "Murder! Murder!" He became incontinent and progressively more stuporous. At that stage a slight hemiparesis, with increased deep tendon reflexes, was noted on the right side. During the last thirty days of his life his temperature was elevated, the pulse rapid and small and respiration stertorous. He died in deep coma on July 13, 1943.

Pathoanatomic Study (Dr. Harry Zimmermann).—"The brain was tremendously distorted, with the biparietal diameter much increased as a result of a tumor in the left parietal lobe and a cerebral hernia in the right parietal region. The left parietal bone flap was adherent to the underlying cortex. The cerebral convolutions of the remainder of the brain were greatly flattened. Gyral herniations into the dura were present over both temporal lobes. The left uncus and the adjacent occipital lobe showed evidence of molding by herniation through the tentorial incisure. There is practically no cerebellar pressure cone. Frontal section through the brain at the level of the anterior commissure disclosed a huge, fungating tumor mass in the greatly dilated inferior horn of the left lateral ventricle. This mass infiltrated most of the structures of the basal ganglia on the left side. The midline of the brain had been shifted to the right. Most of the left parietal, temporal and occipital lobes were replaced by tumor tissue. The tail of the splenium of the corpus callosum was involved by the neoplasm, which extended into the right occipital lobe. In this lobe a large operative cavity was present, the walls of which contained tumor tissue.

"There were a few small, flat, calcified plaques in the meninges of the lower thoracic portion of the cord and near the conus. There was no sign of involvement by the tumor of either the spinal meninges or the cord itself."

All the other findings were normal except for aspiration pneumonia.

Anatomic Diagnosis.—The diagnosis was glioblastoma multiforme, involving both the parieto-occipital region and the basal ganglia (left); healed scars of decompressions (right and left sides); herniation of the brain (right), and aspiration pneumonia.

COMMENT

We were able to observe 6 cases of denial of blindness over a period of eighteen months in a 600 bed hospital. This fact alone demonstrates that the syndrome is not rare, but it is easily overlooked unless the examiner is aware of its existence. One is inclined to believe the statement of the patient who says he can see without an attempt at verification. Furthermore, most examiners are reluctant to make any attempt to stress forcibly to the patient such a severe defect as blindness. All patients who present such a syndrome are deteriorated and have disturbances of retention and orientation, hallucinations and delusions, and neuropsychiatrists may look at their denial of blindness as one of many psychotic manifestations. Moreover, in most cases it is of little practical significance whether these blind patients affirm or deny their blindness, and the syndrome is therefore predominantly of theoretic interest.

The symptoms of the syndrome are fairly uniform, in contrast to the anosognosia of a hemiplegia, which may vary from mere imperception of the weakness to denial of the existence of the paralyzed extremities (Nielsen[19]). The symptoms in our cases, as well as those in all cases described in the literature, may be discussed under the following headings:

1. The patients do not perceive their blindness, act as though they could see, report visual experiences and deny their blindness when confronted with it. 2. All patients show at least a moderate amount of intellectual deterioration. 3. The patients have disturbances of orientation, defects of memory and retention and a tendency to confabulation. 4. All of our patients had an amnestic aphasia. 5. The most frequent cause for the blindness of such patients is bilateral

19. Nielsen, J. M.: Disturbances of the Body Scheme, Bull. Los Angeles Neurol. Soc. **3**:127-136, 1938.

hemianopsia due to occipital or temporoparietal lesions.

One of the most striking features in the behavior of our patients was their inability to learn from their experiences. As they were not aware of their blindness when they walked about, they bumped into the furniture and walls but did not change their behavior. When confronted with their blindness in a rather pointed fashion, they would either deny any visual difficulty or remark: "It is so dark in the room; why don't they turn the light on?"; "I forgot my glasses," or "My vision is not too good, but I can see all right." The patients would not accept any demonstration or assurance which would prove their blindness. The behavior of these persons reminds one of psychotic patients with a fixed delusional system which cannot be refuted. As they refuse to accept rather simple and convincing proofs of their blindness, one is at first inclined to regard their behavior as a mixture of malingering and hysterical reactions as they occur in the Ganser state. However, in their premorbid personality no trace of such tendencies can be found. Of course, one may satisfy oneself with the rather general explanation that their organic cerebral disease is responsible for a regression to more primitive hysterical patterns of behavior, in which the denial of their most important defect is of paramount importance.

All our patients showed considerable intellectual deterioration. This was obvious in clinical examination, in standard intelligence tests and in special examinations designed by Goldstein [20] to test abstract and concrete behavior. The deterioration alone, however, does not adequately explain the denial of blindness. It would be difficult to understand how any degree of intellectual impairment would lead to imperception of the patients' lack of vision. Their inability to learn from experience may be partly explained by their severe impairment of retention. Such a defect of retention and memory for recent events with disorientation and confabulations occurred in all our patients. E. Redlich and Bonvicini [10] noticed it in their own observations but did not stress it as a universal feature from a descriptive point of view. Anton's syndrome may be said to consist of a Korsakoff psychosis in a blind person. The existence of visual hallucinations alone in a blind person does not necessarily constitute Anton's syndrome. Such hallucinations in the blind without denial of blindness are not uncommon in persons with dementia paralytica. In all our patients an amnestic aphasia was present.

Anton's syndrome is not a constant and unchanging phenomenon. This was noted particularly by E. Redlich and Bonvicini [10] and reflects our own experience. Patients like P. K. and A. J. (cases 6 and 3), who suffered from progressive cerebral lesions, showed the syndrome constantly, while others exhibited a good deal of fluctuation in their perception of blindness, as did J. C. (case 4). In J. C. the syndrome was observed only for a few days.

The fluctuations speak somehow against the possibility of strict localization of any lesion which may be responsible for the syndrome. Such fluctuations can be demonstrated in most cortical syndromes, and they speak in favor of holistic interpretations of disturbances of higher cerebral functions, as classified by Goldstein.[21] The question of localization has been discussed by some authors. Anton [1a] did not assume any strict localization but expressed the opinion that imperception of blindness is due to rather generalized lesions in the brain, such as destruction of a major portion of the long association fibers. Thus, impairment of one sensory sphere will not be conveyed to other parts of the brain and imperception of the defect will result. Redlich and Bonvicini [10] were even more general in their statements and assumed that any diffuse cerebral impairment in a blind person may lead to the syndrome, though the majority of patients show lesions of the occipital lobe. Poetzl [12] assumed that the syndrome is due to strictly localized interruptions between thalamic and cortical centers. He claimed such localization in his cases of anosognosia and autotopagnosia, particularly hemiplegia on the left. In case studies Wortis and Dattner,[22] Gerstmann,[23] Nielsen [19] and Olsen and Ruby [24] assumed a similar point of view. Experimental work by Dusser de Barenne and McCulloch [25] and theoretic considerations by Cobb [26] point to the existence of reverberating circuits

20. Goldstein, K.: A Case of Aphasia with Special Reference to the Problems of Repetition and Word Finding, J. Neurol. & Psychiat. **1**:333-341, 1938.

21. Goldstein, K.: The Organism, New York, American Book Company, 1939.

22. Wortis, H., and Dattner, B.: An Analysis of a Somatic Delusion, Psychosom. Med. **4**:319-323, 1942.

23. Gerstmann, J.: Problem of Imperception of Disease and of Impaired Body Territories with Organic Lesions: Relations to Body Scheme and Its Disorders, Arch. Neurol. & Psychiat. **48**: 890-913 (Dec.) 1942.

24. Olsen, C. W., and Ruby, C.: Anosognosia and Autotopagnosia, Arch. Neurol. & Psychiat. **46**:340-344, (Aug.) 1941.

25. Dusser de Barenne, J. G., and McCulloch, W. S.: Direct Functional Interrelation of Sensory Cortex and Optic Thalamus, J. Neurophysiol. **1**:176-185, 1938.

26. Cobb, S.: Borderlands of Psychiatry, Cambridge, Mass., Harvard University Press, 1943.

and interaction between thalamus and sensory cortex which will bring about conscious representation and integration of the sensual spheres. This interaction between thalamus and sensory cortex seems responsible for conscious representation of the body (the body image as Schilder [27] called it) and for conscious experience of the sensual spheres. As Cobb put it, these reverberating circuits between thalamus and sensory cortex are responsible for a state of neural vigilance, awareness of self and environment. One may say that they are responsible for conscious "experiencing." Kahn's [28] thesis that "experiencing" is characteristic of the integrated human organism but is absent in animals, infants and deteriorated and disintegrated patients might find its neurologic substrate by a further study of the normal and impaired function of these reverberating circuits. Bilateral lesions between the visual thalamus and the visual cortex or lesions involving some of their connecting fibers seem to be responsible for an imperception of blindness. Whether such lesions alone will prove to be the cause of an imperception of blindness cannot be stated with certainty because all our patients, in addition to those described in the literature, have shown generalized disease of the brain as well as any such focal lesion.

The causes of blindness in patients who deny their blindness may be varied. Four patients showed bilateral hemianopsia; but 1 patient was blind as the result of secondary optic nerve atrophy, and the amaurosis of another was due to diabetic retinopathy. The cause of the blindness seems to be irrelevant in the pathogenesis of Anton's syndrome, although apparently bilateral hemianopsia is more frequent than the unilateral form. For reasons which are not understood, most persons do not notice a hemianopsia, with the exception of patients with migraine, who report an actual halving of their visual fields. Goldstein studied one aspect of this phenomenon in his treatise on pseudofovea. The last word on this imperception of hemianopsia, particularly of vision obscure and vision nulle of the old French authors, has not been said. One may assume that some patients with bilateral hemianopsia do not perceive their blindness because they do not notice the loss of any part of their vision; i. e., they do not notice their hemianopsia.

At times normal blind persons have a need to disguise their blindness and to act as though they could see. Romain Rolland described such a case in the blind girl in "Jean Christophe." It may be assumed that this tendency will occasionally play a role in cases in which a pathologic condition of the brain exists. Denial of blindness as a pure hysterical symptom has not been observed; disturbances of the body scheme in hysterical states, schizophrenia and symptomatic psychoses are well known and were described by Schilder,[27] Bychowski [29] and others. The syndrome is in some ways the opposite of so-called apperceptive blindness, in which condition the patient is able to see but behaves as though he were blind because he is unable to apperceive "visual impressions of a chaotic outer world" (Patterson and Stengel [30]). Furthermore, the degree of insight which patients with visual agnosias have may vary considerably during the course of the illness (Adler [31]). In 1 patient (J. C.), with a temporary state of deterioration, we thought that psychologic reintegration was accompanied with perception of his blindness. Imperception of blindness undoubtedly is related to the disturbances of the body scheme described as anosognosia and autotopagnosia, and to the imperception of sensory aphasia. Such disturbances may be predominantly due to focal lesions; however, we have not reachced a complete explanation from neurologic studies. In most cases a combined neurologic and psychiatric approach throws some light on such syndromes.

SUMMARY

The blindness of 6 patients presenting the syndrome of denial of their own blindness was caused by diabetic retinopathy, in 1 patient; by atrophy of the optic nerve, in another, and by bilateral hemianopsia due to tumor or to vascular lesions, in 4 patients. Moreover, all patients had diffuse cerebral lesions. All showed intellectual deterioration: disorientation, severe impairment of recent memory and retention, and confabulation. The existence of bilateral focal lesions of the visual radiations or of the occipital visual areas leading to bilateral hemianopsia seems to play an important role in the pathogenesis of the syndrome. The interruptions of reverberating circuits between the thalamus and the sensory cortex constitute the outstanding etiologic factor.

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SYNKINETIC PUPILLARY PHENOMENA AND THE ARGYLL ROBERTSON PUPIL

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From time to time the Argyll Robertson pupil has been attributed to a lesion outside the central nervous system, as in the oculomotor nerve, the ciliary ganglion or the ciliary nerves. The most recent proponents of this theory are Nathan and Turner.[1] On the basis of 2 cases of their own and of 8 cases collected from the literature, they concluded that the Argyll Robertson pupil may be caused by damage to the peripheral efferent pathway to the iris. They also argued that there must be two efferent routes for pupillary constriction. "Parasympathetic pupillo-constrictor fibers relay not only in the . . . cells of the ciliary ganglion but also in the more peripherally situated episcleral ganglia." All their evidence, however, was casuistic, and their observations were not complete.

Although they constantly dealt with the problem, they neglected to mention the common diagnostic signs of the Argyll Robertson pupil, which are miosis, pupillary inactivity to light but constriction on convergence, and poor dilator response to locally instilled mydriatics. None of their cases had all these essential features. The criteria that Nathan and Turner set for themselves were as follows:

> (*a*) The pupil on the normal side must contract when the affected side is stimulated; (*b*) the affected pupil must not contract to light or dilate in darkness either directly or consensually; (*c*) both pupils must contract normally on accommodation and convergence . . . and (*d*) the lesion should be known to be peripheral.

In offering explanations for these abnormal pupillary reactions, they indirectly considered the possibility that nerve regeneration might produce synkinesias, which, in turn, would lead to pupillary constriction on convergence but not in reaction to light. They declared that the voluntary acts of accommodation and convergence may evoke a contraction of the pupil which is much stronger than the response to light reflex and that this difference should be most apparent in patients with lesions of the oculomotor nerve. Then they argued that if the so-called Argyll Robertson pupil following trauma to the oculomotor nerve were due to nerve regeneration, patients recovering from peripheral oculomotor palsy should reveal signs of an Argyll Robertson pupil, but they stated that this does not occur. The latter statement is not entirely correct. Pupillary constriction in association with ocular movements following recovery from oculomotor ophthalmoplegia does occur, and cases have been described.[2] A careful search for pupillary synkinesias will reveal them to be present in many cases of oculomotor paralysis. It is apparent that these authors did not seriously consider the possibility that such pupillary synkinesias could account for the so-called Argyll Robertson pupil. If they had, they would have stressed the fact that various movements of the eyes did or did not produce a change in the diameter of the affected pupil. Since such observations were not mentioned in their report, it is doubted whether Nathan and Turner were dealing with the classic syndrome of the Argyll Robertson pupil.

Personal observations have disclosed that the constriction in the so-called Argyll Robertson pupil following peripheral lesions of the oculomotor nerve is present not only on convergence but on downward, upward and inward movements of the ipsilateral globe. The following clinical and experimental data are reported to show that pupillary constriction on convergence may be one of several synkinesias following lesions of the oculomotor nerve.

CLINICAL DATA

CASE 1.—L. F. L., a 20 year old radio man, second class, accidentally fell from flight to hangar deck. He sustained fractures of the skull and the right femur and was unconscious for several hours. He was given emergency treatment; when he regained consciousness

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1. Nathan, P. W., and Turner, J. W. A.: Efferent Pathway for Pupillary Contraction, Brain **65**:343-351 (Dec.) 1942.

2. Bender, M. B., and Alpert, S.: Abnormal Ocular and Pupillary Movements Following Oculomotor Paralysis, Arch. Ophth. **18**:411-414 (Sept.) 1937.

ness, complete paralysis of the right oculomotor nerve was noted. The pupil was dilated and fixed to all forms of stimuli. The eyeball was deviated externally. All external ocular muscles but the superior oblique and the lateral rectus were paralyzed. A roentgenogram of the skull revealed a stellate fracture involving the right frontal bone and the sphenoid sinus.

Ten weeks after the injury, examination revealed bilateral anosmia and, in the right eye, impaired visual acuity, optic nerve atrophy, narrowing of the palpebral fissure, due to enophthalmos, and a greatly diminished corneal reflex. The ptosis disappeared, and all the ocular movements returned and appeared to be normal in the formerly affected eye. The left pupil reacted well directly and consensually to light and contracted on convergence. The right pupil measured 5 mm. in diameter and did not react directly or consensually to light stimuli. It did not dilate in the dark. This pupil contracted to a diameter of 2 mm. when the eyeball was directed downward or toward the nose. The contraction was also present on inward and, to a lesser extent, on upward gaze. The best pupillary constriction in the right eye was found to occur on downward movement of the globe. Strong closure of the lids of this eye also produced contraction of the right pupil. The right pupil dilated with atropine.

Three months after the injury there was subjective improvement. Reexamination disclosed the same findings as on previous occasions except for apparent improvement in his visual acuity, especially at a near point. However, the patient was able to see print clearly at a near point only when his affected eye was deviated in the inward, downward, upward or convergent position. Outward deviation of this eye was without effect on vision. In summary, any contraction of the formerly ophthalmoplegic muscles produced associated improvement in vision at a near point. From this it may be concluded that the apparent improvement in visual acuity was the result of synkinetic contraction of the formerly paralyzed ciliary muscle.

This case is practically identical with the cases described by Nathan and Turner and meets all their criteria. It is an example of oculomotor ophthalmoplegia with rapid but incomplete recovery, with iridoparesis and associated synkinetic phenomena as residua. On contraction of any of the formerly paralytic extraocular muscles, especially the inferior rectus, the sphincter pupillae contracted simultaneously. If this pupil were examined only for the conventional reactions to light and on convergence, the clinical picture would simulate the Argyll Robertson pupil.

Another interesting finding in this case was the synkinetic contraction of the ciliary muscle in association with action of any of the formerly ophthalmoplegic muscles.

Case 2.—J. T. A., a 23 year old electrician's mate, first class, was injured in a motorcycle accident. He was admitted to the hospital in an unconscious state and was treated conservatively. Two days after admission he was still comatose. Lumbar puncture at this time disclosed cloudy fluid, which contained 2,600 white blood cells, with 90 per cent polymorphonuclear leukocytes. He had all the clinical signs of complicating pyogenic meningitis. With penicillin and sulfadiazine therapy he improved, so that two days after treatment with the chemical he regained consciousness. At this time it was noted he was unable to raise either eyelid. The left eye was blind. There was paralysis of all movements in both eyes, except for abduction of the right eye. A roentgenogram of the skull disclosed a fine fracture line in the left frontal sinus.

Three weeks after the injury, slight movements of each eyeball appeared, and the ptosis lessened. This improvement progressed, so that eight weeks after the injury the ocular status was as follows: Both eyes were in a divergent position, and both superior lids were partially drooped. In the left eye there was no light perception and the optic nerve appeared atrophied. Vision in the right eye was 10/10. Except for bilateral paresis of the internal rectus muscle and convergence palsy, all ocular movements were normal. The left pupil measured 4 mm. and the right pupil 3.5 mm. These measurements were made in sunlight and were found to be the same in semidarkness. Neither pupil reacted to strong light, directly or consensually. There was no dilatation in darkness. Both pupils contracted almost to a pinpoint on downward movement or on attempted convergence and to a lesser extent on upward movement. Each pupil contracted with attempted movement of the tested eye. There was no visible retraction of the superior lids on downward gaze. Both pupils dilated maximally with atropine.

This case is another example of recovery from oculomotor ophthalmoplegia with residual paralysis to stimulation with light and synkinetic constriction of the pupils. Were it not for the pupillary contractions in association with ocular movements other than convergence, the clinical picture would strongly simulate the syndrome described by Argyll Robertson. It is interesting and significant that in this case and in the preceding case practically all of the formerly paralyzed external ocular muscles recovered. Only the sphincter pupillae remained paretic, being inactive to light but contracting in association with movements of the eyes.

Recovery from oculomotor ophthalmoplegia does not always occur in this manner. In some instances the postophthalmoplegic synkinesias are manifest not only in the pupil but in the formerly ptosed superior eyelid, so that the eyelid retracts in association with attempted downward movement of the globe.

Case 3.—A 42 year old woman[3] was admitted to the hospital clinic with signs of paralysis of the third, fourth and fifth cranial nerves on the left side. The causative factor was syphilis. With antisyphilitic therapy she showed progressive improvement. Fourteen weeks after the onset of the palsies there were partial recovery of adduction movements of the left eye. The left pupil, which was at first fully dilated, became small. This pupil did not react directly or consensually to light but contracted on attempted convergence. However, the pupil was also observed to contract in association with attempted downward, inward and upward movement of the left globe. Another synkinetic phenomenon was found in conjunction with the movements

3. This patient was observed at the Mount Sinai Hospital, New York.

of this globe. Not only did the pupil contract, but the partially ptotic superior eyelid retracted synkinetically on attempted convergence, downward or inward movement of the left eye.

In this case of syphilis, had it not been for the synkinetic phenomena, the left pupil would have been readily classified as the Argyll Robertson type. In this case the synkinetic phenomena were apparent not only in the sphincter pupillae muscle but in the superior eyelid. The retraction of the eyelid in association with ocular movements has been called the pseudo-Graefe phenomenon.[4]

EXPERIMENTAL DATA

The so-called pseudo-Graefe phenomenon, or retraction of the superior lid in association with downward movement of the eye, is a synkinesia which is invariably found on recovery from ophthalmoplegia due to section of the intracranial portion of the oculomotor nerve in the monkey and the chimpanzee.[5] In some of these monkeys the pupil which is fixed to light contracts on convergence, adduction or downward or upward movement of the affected eye ten weeks after the ophthalmoplegia is experimentally produced. The following is a condensed protocol of observations made on a monkey.[6]

Experiment 1.—The subject of the experiment was a young male Macaca mulatta, weighing 2,800 Gm. The ocular reactions were normal.

Operation (Oct. 20, 1936).—A large bone flap, extending beyond the midline, was turned down on the left side, and, by gentle elevation of the temporal lobe, the optic and oculomotor nerves, the pituitary stalk and the cavernous sinus were brought into view. The oculomotor nerve was then cut with long-handled scissors, and the two ends were drawn apart 2 to 3 mm.

Postoperative Notes.—At the end of the operation the left pupil was dilated, and when the monkey began to recover from the anesthesia, the total oculomotor ophthalmoplegia of the left eye became apparent. The next day the left eyelid exhibited complete ptosis, with external deviation of the globe. The only movement remaining was outward deviation (external rectus muscle). The left pupil was dilated and "fixed" to all forms of stimulation with light.

Sixth Day: The ptosis began to diminish.

Twenty-Second Day: The ptosis was less apparent. The margin of the left upper eyelid was at the upper pole of the maximally dilated pupil.

Twenty-Eighth Day: When the monkey looked down with its right eye, its right eyelid descended synchronously; there was no downward movement of the left eyeball and none of the eyelid (earliest manifestation of the pseudo-Graefe sign). Downward movement of both superior eyelids was noted during spontaneous blinking and in response to visual or corneal stimulation.

Thirtieth Day: When the monkey looked down with its right eye, the left upper eyelid retracted. This was the first sign of recovery of muscular movement (a synkinetic response).

Thirty-Second Day: Slight action of the internal rectus muscle was noted in the left eye, the globe being adducted slightly beyond the midline in conjugate gaze to the right.

Thirty-Fourth Day: Ptosis had completely disappeared.

Thirty-Sixth Day: A slight decrease in pupillary diameter was observed.

Forty-First Day: Action of the internal rectus muscle had completely returned, the left eyeball moving well inward in horizontal excursions. The left pupil was still dilated to a diameter of 6 mm. and was inactive to light.

Forty-Ninth Day: When the animal looked to the right, both globes moved equally well in the horizontal plane, but the left superior eyelid retracted and the left globe moved slightly inward.

Seventy-Sixth Day: The diameter of the left pupil had been reduced to 3 mm. The only visible motion in the left eye was in the horizontal plane. The left pupil exhibited some decrease in diameter in association with fixation at a near point, but there was no response to light (sign of synkinetic constriction of the pupil).

Second Operation (seventy-seventh day, Jan. 5, 1937).—Stimulation of the cervical portion of the left sympathetic trunk with the animal under anesthesia induced with sodium amytal caused dilation of the left pupil, slight exophthalmos and some retraction of both the upper and the lower eyelid. The sympathetic trunk was then resected and the superior cervical ganglion crushed.

Postoperative Notes.—First Day: Piloparalysis on the left side of the face was conspicuous. The left pupil was 2 mm. in diameter and did not react to light. The pseudo-Graefe sign (synkinetic retraction of the lid) was still present. There was some enophthalmos, with secondary elevation of the edge of the lower lid, but no true ptosis.

Seventh Day: When the monkey looked down with the right eye, the left upper eyelid moved up, while the left globe move inward. When he looked up with his right eye, the left eyeball moved slightly inward, while the left pupil constricted to a slight degree (synkinetic phenomena). Direct and consensual response to light was still absent in the left pupil.

Thirteenth Day: When the animal looked at a point near or to the right, requiring action of the left internal rectus muscle, the left pupil contracted from 3 to 1.5 mm. in diameter (synkinetic phenomenon). There was no reaction to light.

Fortieth Day: When the lids closed, there were a slight contraction of the left pupil and more pronounced contraction of the right pupil (lid closure reflex).[6a] Bell's phenomenon was not observed.

Fifty-Fifth Day: The left pupil was 4 mm. in diameter.

Fifty-Sixth Day: The left pupil was 3.5 mm. in diameter.

4. Bender, M. B.: The Nerve Supply to the Orbicularis Muscle and the Physiology of Movements of the Upper Eyelid (with Particular Reference to the Pseudo-Graefe Phenomenon), Arch. Ophth. **15**:21-30 (Jan.) 1936.

5. Bender, M. B., and Fulton, J. F.: Factors in Functional Recovery Following Section of the Oculomotor Nerve in Monkeys, J. Neurol. & Psychiat. **2**: 285-292 (Oct.) 1939; Functional Recovery in Ocular Muscles of a Chimpanzee After Section of the Oculomotor Nerve, J. Neurophysiol. **1**:144-151 (March) 1938.

6. These experiments were performed in the laboratory of physiology, Yale University, New Haven, Conn.

6a. Bender, M. B.: Eyelid Closure Reaction; Arch. Ophth. **29**:435-440 (March) 1943.

Sixtieth Day: The left pupil was 2.5 mm. in diameter.

Sixty-First Day: The left pupil contracted from 2.5 to 1.5 mm. in association with convergence. It still did not react to light. In this respect the left pupil had the characteristics of an Argyll Robertson pupil.

Seventy-First Day: The diameter of the left pupil remained at 2.5 mm. The pupil did not dilate in the dark. When the monkey attempted to look down, up or to the right, the abnormal movements of the upper eyelid and the internal rectus muscle of the left eye were evident, and the apparent Argyll Robertson phenomenon was also manifest.

Third Operation (seventy-ninth day, March 26, 1937).—The bone flap was reelevated and the reunited left oculomotor nerve again severed.

Postoperative Notes.—First Day: Ophthalmoplegia was complete in the left eye, as after the first operation.

Third Day: Ptosis on the left side was incomplete; the pupil was 6 mm. in diameter and was fixed to all forms of stimuli, and the globe could be abducted but not adducted.

Tenth Day: The left palpebral fissure was 5 mm. wide. No change in the left pupil was evident.

Twenty-Fifth Day: The ptosis was half complete. The left pupil measured 4.5 mm. in diameter.

Thirty-Fifth Day: The left palpebral fissure was almost completely open, and the pseudo-Graefe sign was apparent. The left eyeball could be adducted slightly beyond the midline.

Thirty-Eighth Day: There was complete recovery in power of elevating the left lid and in adduction of the globe.

Forty-First Day: When the right eye looked down, the left upper eyelid moved up, and the left eyeball moved slightly inward. The left pupil measured 4 mm. in diameter.

Sixty-Third Day: When the left eye moved nasally the left pupil became smaller. The pupil also contracted slightly when the monkey fixated at a near point.

Eighty-Sixth Day: The left pupil was 3.5 mm. in diameter. It contracted slightly in association with closure of the lids.

One Hundred and Twenty-Fifth Day: The left pupil was observed under a magnifying glass and was found to contract in association with fixation at a near point, on adduction of the globe and with closure of the lids. Synkinetic phenomena were also present in the left upper lid on downward movement of the globe. The ocular status at this time revealed upward movements in the left upper eyelid which were synchronous with action of the internal rectus muscle and with vertical (up and down) or dextral movements of the normal right eye. Vertical movements in the left eye were absent.[7]

Two Hundred and Seventy-Eighth Day: The left pupil showed a definite reaction to light.

Four Hundred and Fortieth Day: The ocular status was unchanged. The left pupil failed to enlarge in low illumination.

7. Recovery of vertical movements in the affected eye was never apparent. This, however, did not mean that the elevators or depressors of the globe remained paralyzed; on the contrary, the absence of upward or downward movements was due to simultaneous contraction in the elevators and depressors of the eye, which resulted in absence of movement. When in the eye recovering from ophthalmoplegia the inferior rectus muscle had been previously cut upward movements of the globe became apparent; that is, as soon as one of the antagonists was eliminated the action of the other became apparent.

These experiments show that the syndrome simulating the Argyll Robertson pupil may be reproduced in the monkey by sectioning the oculomotor nerve intracranially and permitting regeneration to take place. The signs of regeneration are (1) recovery of adduction, (2) synkinetic retraction of the superior lid in association with attempted downward, upward or inward movement of the formerly ophthalmoplegic eye and (3) synkinetic contraction of the pupil. This pupil, which becomes progressively miotic during the period of recovery, does not react directly or consensually to light but contracts conspicuously in association with attempted vertical and inward movements of the affected globe.

That these pupillary reactions are not due to structural changes in the ciliary ganglion or the ciliary nerves is borne out by the fact that the oculomotor nerve was twice cut intracranially and that the apparent Argyll Robertson pupil became manifest each time after a definite interval in the stage of recovery from the ophthalmoplegia.

Experiment 2.—Pupilloconstrictor fibers are known to course in the ciliary nerves. The theory that another pupilloconstrictor pathway may exist in other branches of the oculomotor nerve, such as those innervating the inferior rectus and inferior oblique muscles, is refuted by the following simple experiment. Intraorbital section of the branches of the oculomotor nerve other than the ciliary nerves produced no changes in the pupil. The pupil in the monkey employed reacted well to light and on convergence. Subsequent intracranial section of the ipsilateral oculomotor nerve in the same monkey produced the pupillary effects described in experiment 1. In other words, there appears to be no basis for the claim that some of the pupilloconstrictor fibers may travel through the inferior branches of the oculomotor nerve, external to the ciliary ganglion.

Experiment 3.—Intraorbital section of the ciliary ganglion or the ciliary nerves alone or in combination with destruction of the adjacent optic nerve in the monkey or cat produced complete iridoplegia with no constriction to light or in convergence. However, eight to ten weeks after this section there were signs of nerve regeneration. The pupil began to react well both directly and consensually to light and to contract on convergence.[8] There was no difference between the reaction to light and the response on convergence. There were no signs suggestive of the Argyll Robertson pupil.

Experiment 4.—A partial lesion, such as section of the superior fibers of the oculomotor nerve trunk in its intracranial course, produced complete but transient ophthalmoplegia in the monkey. This was followed by rapid recovery in all functions of the external ocular muscles. The sphincter pupillae, however, remained paretic for a longer time. In 1 monkey with such an experimental lesion there was almost complete recovery from the ophthalmoplegia on the fifteenth postoperative day. There was no ptosis, and downward, upward and

8. In cases in which the adjacent optic nerve was crushed, the direct reaction to light remained lost while the consensual response was restored.

inward motion of the globe appeared normal. However, the pupil, which measured 6 mm. in diameter, was fixed to light. On the thirtieth postoperative day the pupil, smaller in diameter, began to react sluggishly to light both directly and consensually; the pupillary constriction on convergence seemed to be brisker than that to light. In other words, regeneration or recovery from oculomotor ophthalmoplegia appeared to be most retarded in pupillary reaction to stimulation with light. Noteworthy was the absence of ocular synkinesis in the monkey with incomplete section of the oculomotor nerve.

COMMENT

The clinical and experimental data herewith presented clearly indicate that the pupillary changes which appear after an oculomotor ophthalmoplegia are not the typical reactions found with the classic Argyll Robertson pupil. Although such a pupil is fixed to light, it reacts not only on convergence but in association with internal and vertical movements of the affected eye.

It may be asked why the postophthalmoplegic pupil reacts on convergence but not to light. This may be due to the fact that light, which is a relatively weak stimulus, does not produce a reflex motor response sufficiently strong to penetrate the functional block caused by the scar in the healing oculomotor nerve trunk.[9] On the other hand, the motor energy evoked by the act of convergence, or by a strong attempt at vertical or internal movement of the eye, is adequate for the impulse to pass through the scar to all the regenerated axon fibers. Since the newly formed axis-cylinders branch freely and grow indiscriminately into the distal stump, it is readily understood why an impulse intended for one group of muscles may be shunted at the scar via the regenerated nerve fibrils to other muscle masses.[10] Thus, an impulse to the internal, the inferior or the superior rectus muscle may cause widespread contractions so that all the muscles supplied by the formerly injured oculomotor nerve act simultaneously. Whether all muscles contract to an equal degree depends on the extent of the lesion, the number of nerve fibers regenerated, how extensively the regenerated axis-cylinders branch and how much nerve energy is discharged into the oculomotor nerve.

The pupillary constriction found in association with movements of the globe may not be of the same degree for each of the individual movements. Thus, it has been found that in some cases the pupil contracts only in association with downward gaze, or only with internal movements of the eye or on convergence. In still other cases the pupil contracts on attempted upward gaze or with movements in any direction or directions effected by the recovered ocular muscles. The type and degree of pupillary constriction vary with the mode of regeneration and with other factors previously stated. From these clinical and experimental observations, it is apparent that the so-called Argyll Robertson pupil which occurs after a lesion in the oculomotor nerve is due to partial regeneration of fibers to the sphincter pupillae muscle and synkinetic contraction of the iris in association with movements in the rest of the eyeball. Consequently, it is erroneous to classify this pupil as the one described by Argyll Robertson. If, for the sake of brevity or expressive meaning, an eponym is preferred, the term "pseudo Argyll Robertson pupil" may be employed, just as "pseudo-Graefe sign" is used to denote synkinetic retraction of the lid.

SUMMARY

After an oculomotor ophthalmoplegia the iris may be found to contract on convergence but not to light, thus simulating the Argyll Robertson pupil. Closer examination, however, discloses that this pupil reacts not only on convergence, but synkinetically with other movements, namely, downward, inward or upward movement of the affected globe. The synkinetic pupillary constriction may sometimes be associated with synkinetic retraction of the lid. The phenomena of synkinetic pupillary constriction and retraction of the eyelid can be reproduced experimentally by intracranial section of the oculomotor nerve in the monkey. These phenomena are partly explained by the theory of indiscriminate regeneration of oculomotor nerve fibers. It is concluded that the so-called, or pseudo, Argyll Robertson pupil, sometimes noted after head injury with a complicating oculomotor ophthalmoplegia, has no etiologic relationship to the classic pupillary reaction originally described by Argyll Robertson.

9. In the experimental monkey, the threshold of an electrical stimulus necessary to evoke a contraction of an ocular muscle or pupillary constriction is much higher in that part of the regenerated oculomotor nerve which runs to the scar than in the part which leaves it. Apparently, the scar partially blocks the impulses originating in the nucleus of the oculomotor nerve.

10. To account for the synkinetic contractions which follow regeneration of the oculomotor or the facial nerve, consideration must be given to the functional and anatomic changes which may accompany regeneration in the entire motor neuron unit in question. The changes may occur at the ganglion cell body, at the nerve scar or at the motor end plate and muscle. The probability is that all the points mentioned are involved, but most of the experimental evidence at hand indicates that the chief cause of the synkinetic phenomena is the indiscriminate regeneration of axis-cylinders at the scar. Bender.[5]

LATERAL SPINOTHALAMIC TRACT AND ASSOCIATED TRACTS IN MAN

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The whole problem of peripheral pain reception and central pain perception and representation remains one of the fundamental fields of investigation in neurophysiology and clinical neurology. Certain aspects of the problem are of considerable interest to the neurosurgeon. For many patients suffering from persistent intractable pain of organic origin, interruption of the central pain pathways offers a palliative measure. Because dorsal root section severs all afferent paths to the spinal cord, the most successful central interruption is obtained by cutting the lateral spinothalamic tract somewhere along its course. Its relatively superficial position renders it accessible to anterolateral chordotomy, to an incision dorsolateral to the inferior olivary nucleus or to an incision at the lateral sulcus of the mesencephalon. The literature concerning this neurosurgical field has been extensively reviewed,[1] and only pertinent references will be included here.

These neurosurgical procedures depend partly for their success on an accurate anatomic knowledge of the pathways concerned. Clinical and experimental evidence indicates that painful stimuli affect free nerve endings and that the resulting impulses travel centrally over nonmyelinated and myelinated processes of unipolar cells in cerebrospinal ganglia. The central processes of these cells enter the spinal tract of the trigeminal nerve or the dorsolateral fasciculus of the spinal cord. The central path in the spinal cord probably originates from large cells in the dorsal gray matter of the opposite side and, to some extent, of the same side[2] and ascends in the lateral funiculus as the lateral spinothalamic tract, in close association with the spinotectal and the dorsal and ventral spinocerebellar tracts. Approximately the same path is followed by impulses originating from thermal stimuli, although the initial receptors are more complex.

There are certain anatomic and physiologic points concerning this pathway which need clarification.

1. It is not certain how large the axons of the central pain path may be, or how much change occurs after the first and subsequent synapses. It has been stated that the lateral spinothalamic tract contains axons more heavily myelinated than the axons in the peripheral paths.[3] It would be of fundamental interest to know that there are actually more heavily myelinated axons centrally than peripherally. The presence of numbers of nonmyelinated axons in the lateral spinothalamic tract might well lead to false impressions of its size and location if such impressions were based entirely on the Marchi reaction.

2. Although it seems fairly well established that the decussation of fibers in this tract occurs in about one segment,[2] further studies on this point would be valuable in establishing the range of variation, particularly in upper and lower levels of the cord.

3. The degree of lamination within the tract remains to be more definitely determined. It is also thought that axons carrying impulses due to thermal stimuli ascend in the lateral spinothalamic tract, but the extent to which these axons are segregated is still uncertain.

4. Apparently not all the axons in this tract go directly to the thalamus.[4] Some impulses are said to ascend by means of a series of short

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1. (*a*) Grant, F. C.: Surgical Methods for the Relief of Pain, J. A. M. A. **116**:567-571 (Feb. 15) 1941. (*b*) Rasmussen, A. T., and Peyton, W. T.: The Location of the Lateral Spinothalamic Tract in the Brain Stem of Man, Surgery **10**:699-710 (Nov.) 1941. (*c*) Schwartz, H. G., and O'Leary, J. L.: Section of the Spinothalamic Tract at the Level of the Inferior Olive, Arch. Neurol. & Psychiat. **47**:293-304 (Feb.) 1942. (*d*) Walker, A. E.: The Spinothalamic Tract in Man, ibid. **43**:284-298 (Feb.) 1940.

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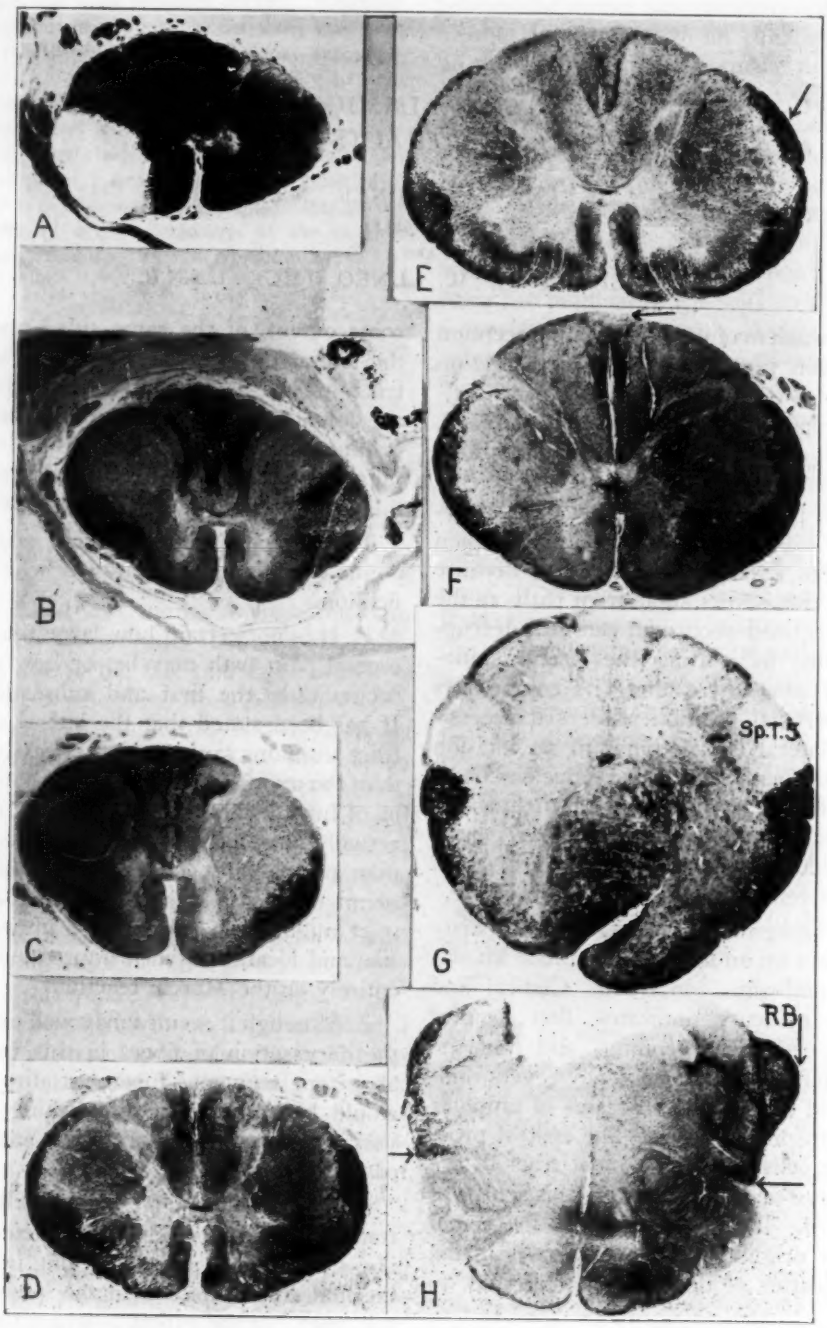

Fig. 1.—Unretouched photographs of cross sections of the spinal cord, the left side throughout corresponding to the left side of the page.

A, a section through the sixth thoracic segment. The lesion on the left side is confined to the lateral funiculus. Weigert method; × 4.5.

B, section through the fifth thoracic segment of the cord, between the two lesions. On the left side is a compact area of degenerating fibers ascending from the lower lesion. On the right side is a more scattered area of degenerating fibers descending from the upper incision. Degeneration resulting from the tabetic process is present in the posterior funiculi. Marchi method; × 4.5.

C, section from the third thoracic segment of the cord. The degeneration on both sides is confined to the lateral funiculi and includes lateral spinothalamic, spinotectal and dorsal and ventral spinocerebellar fibers. Marchi method; × 4.5.

D, section from the second thoracic segment of the cord, in which the increasing concentration on the surface and the dorsal shifting of dorsal spinocerebellar fibers are apparent. Marchi method; × 4.5.

(Legends continued on opposite page)

chains, which are probably situated in the gray matter. Previous observations indicate that after chordotomy the number of degenerating axons decreases rostrally.[1b]

5. The extent of bilateral representation is uncertain. Unilateral chordotomy fails to abolish pain completely, especially in viscera, so that when visceral pain is present bilateral chordotomy is usually necessary. Even then, according to Foerster and Gagel,[2] pain may return, and to explain this they postulated the development of accessory paths in the posterior funiculi.

Any single morphologic or physiologic method is inadequate to settle these points completely. Certain questions, however, such as the exact topography and lamination of the lateral spinothalamic tract, the amount of its ascent while decussating and the degree of intermingling with other tracts can be much more definitely settled if all available human material is adequately studied and reported. Unfortunately, for human material the Marchi stain is the best available morphologic technic. The well known faults of this technic, as well as the infrequency with which cases come to autopsy at the optimum time interval, set a limit on the usefulness of this method. As yet, too few cases have been reported to permit definite knowledge even of the normal range of variation.

MATERIALS AND METHODS

This report is based on a study of the spinal cord and brain stem of a man aged 57 who had a bilateral chordotomy for relief of pains in the legs and tabetic crises. The lesions were made in the upper thoracic portion of the cord, at the sixth thoracic segment on the left side and between the fourth and the fifth thoracic segment on the right side. After operation there was subjective relief of all pain in the legs and gastric crises. In addition, there was loss of pain and temperature sense up to the sixth thoracic dermatomal area on the left side and to the seventh thoracic dermatomal area on the right side. After operation the patient's course was progressively downhill. Pyelonephritis, cortical abscesses of both kidneys and probable uremia developed. All these complications apparently originated from chronic tabetic paresis of the bladder. The patient died twenty-one days after the operation, an interval with the time range of an optimum Marchi reaction in man.

The brain and spinal cord were removed about six hours after death and fixed by immersion in a 10 per cent concentration of solution of formaldehyde U. S. P. Subsequently, selected levels of the spinal cord and brain stem were cut into slices 2 to 3 mm. thick and prepared by the Swank-Davenport[5] modification of the Marchi technic. The slices were dehydrated, embedded in pyroxylin of low viscosity and cut transversely at 60 microns. In general, this method is excellent, and the background is usually free of troublesome artefacts. In this case there was some precipitation of osmic acid in normal areas, particularly in the heavily myelinated tracts of the brain stem, but the areas of true degeneration were sharply outlined and easily followed throughout the spinal cord and the brain stem.

Other slices of the brain stem were dehydrated, embedded in either paraffin or pyroxylin and, after being sectioned, stained with iron hematoxylin, cresyl violet, the activated silver albumose method of Bodian or the Mallory-azocarmine method.

The smallest sections were photographed directly. The largest sections were projected on to drawing material at a magnification of six to eight and the sections outlined. The degeneration was indicated by stippling, the process being checked by microscopic examination. In addition, the areas which were stippled in were photographed directly at higher magnifications.

RESULTS

In this case the chordotomy on each side was performed by inserting the knife at the denticulate ligament to a depth of 4 mm. and bringing it out at the line of exit of the ventral root fibers. Weigert stains of sections from the operative levels indicated that the incisions were confined to the lateral funiculi (fig. 1 *A*). Marchi stains of sections between the two incisions contained descending degeneration on the right side, while ascending degenerating fibers from the lower incision could be clearly seen in the lateral funiculus on the left side (fig. 1 *B*). The descending degeneration lessened as the fibers shifted medially toward the gray matter in lower segments, indicating that the degeneration was due mainly to the interruption of bulbospinal fibers. No major involvement of the pyramidal tracts was apparent on either

5. Swank, R. L., and Davenport, H. A.: Chlorate-Osmic-Formalin Method for Staining Degenerating Myelin, Stain Technol. **10**:87-90 (July) 1935.

E, section from the fifth cervical segment. The degeneration in the lateral funiculi occupies a surface position, and the dorsal spinocerebellar tract (indicated by the arrow) is clearly evident. Marchi method; × 4.5.

F, section from the second cervical segment. The degenerating fibers extend between the dorsal and the ventral roots on the surface. The tendency of degeneration in the posterior funiculi to ascend in the fasciculus gracilis is indicated by the arrow. Marchi method; × 4.5.

G, section at the level of the pyramidal decussation. The compact areas of degeneration immediately ventral to the spinal tract and nucleus of the trigeminal nerve, *Sp. Tr. 5*, on each side are sharply delineated. Marchi method; × 4.5.

H, section through the inferior olivary nuclei. The dorsal spinocerebellar fibers are entering the restiform bodies, *R B*. This section corresponds to the drawing in figure 3 *A*, and the positions of the lateral spinothalamic tracts are indicated by the arrows. Marchi method; × 3.

side. In a section immediately above the incision on the right side (fig. 1 *C*) the degeneration occupied an area corresponding but roughly to the area interrupted by the knife, but still confined to the lateral funiculus. Differentiation here between the lateral spinothalamic and other tracts was not possible. In sections through higher levels of the spinal cord, shifting of the involved fibers toward the periphery was practically identical on the two sides, except that the degeneration resulting from the more rostrally placed incision on the right side was somewhat heavier (fig. 1 *D* to *F*). In addition to this clearly indicated lamination, there was a tendency at cervical levels to a shifting dorsally of what were apparently dorsal spinocerebellar fibers (fig. 1 *E* and *F*). On entering the medulla the fibers became concentrated, and in a section through the decussation of the pyramids the degeneration was crowded into a relatively small area immediately ventral to the spinal tract and nucleus of the trigeminal nerve on each side (fig. 1 *G*). These tracts were actually more compact here than at any other part of their course through the brain stem.

Degenerating fibers were present in the posterior funiculi throughout the cord (fig. 1 *B* to *F*), and these were a result of the tabetic process. The complete destruction of other fibers due to the chronic process is illustrated in the sections stained by the Weigert method shown in figure 2, *A* and *B*. This degeneration could be traced into the medulla, particularly to the nuclei of the fasciculi graciles, but was not apparent in the medial lemnisci.

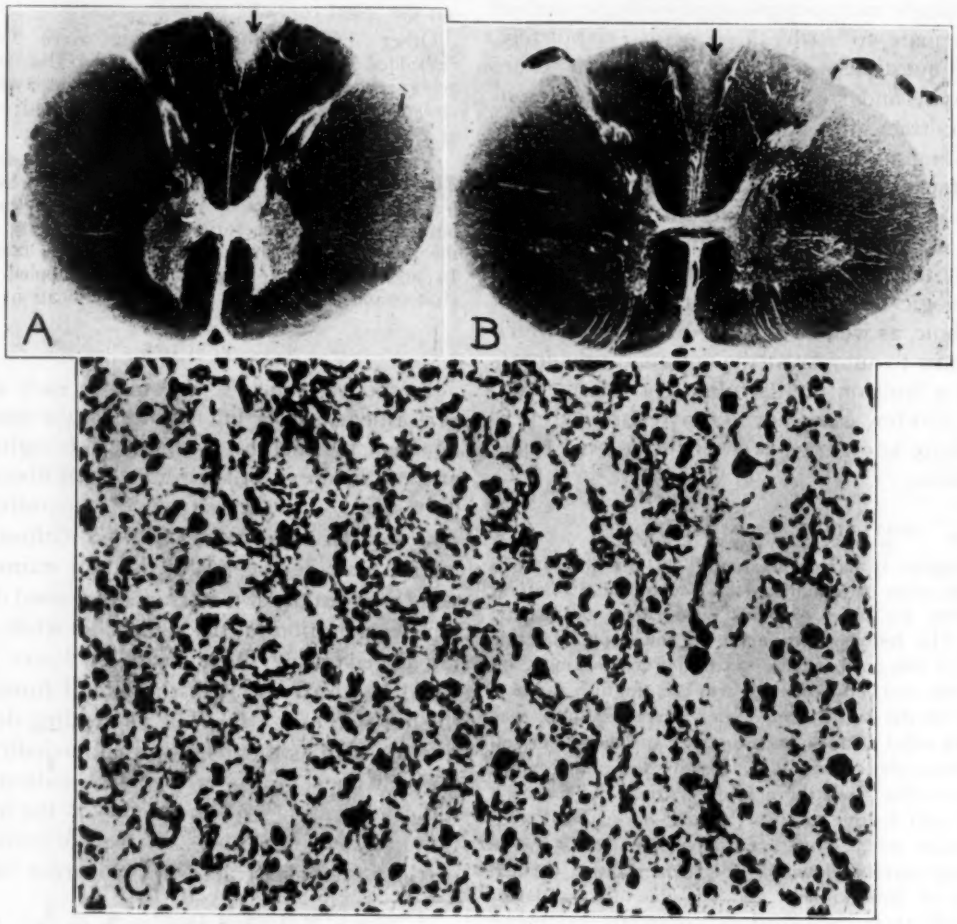

Fig. 2.—*A*, cross section through the first cervical segment, illustrating the degeneration in the fasciculi graciles (arrow). Weigert method; × 6.

B, cross section through the fifth cervical segment of the cord, illustrating peripheral degeneration in the lateral funiculi, as well as degeneration in the fasciculi graciles (arrow). Weigert method; × 6.

C, photomicrograph of the area occupied by the lateral spinothalamic tract. This section is from the second thoracic segment and therefore contains normal fibers. It illustrates the relatively large numbers of nonmyelinated and small myelinated axons in this area. It is not possible to say, however, that these axons actually belong to the lateral spinothalamic tract. Bodian's activated silver albumose method; × 400.

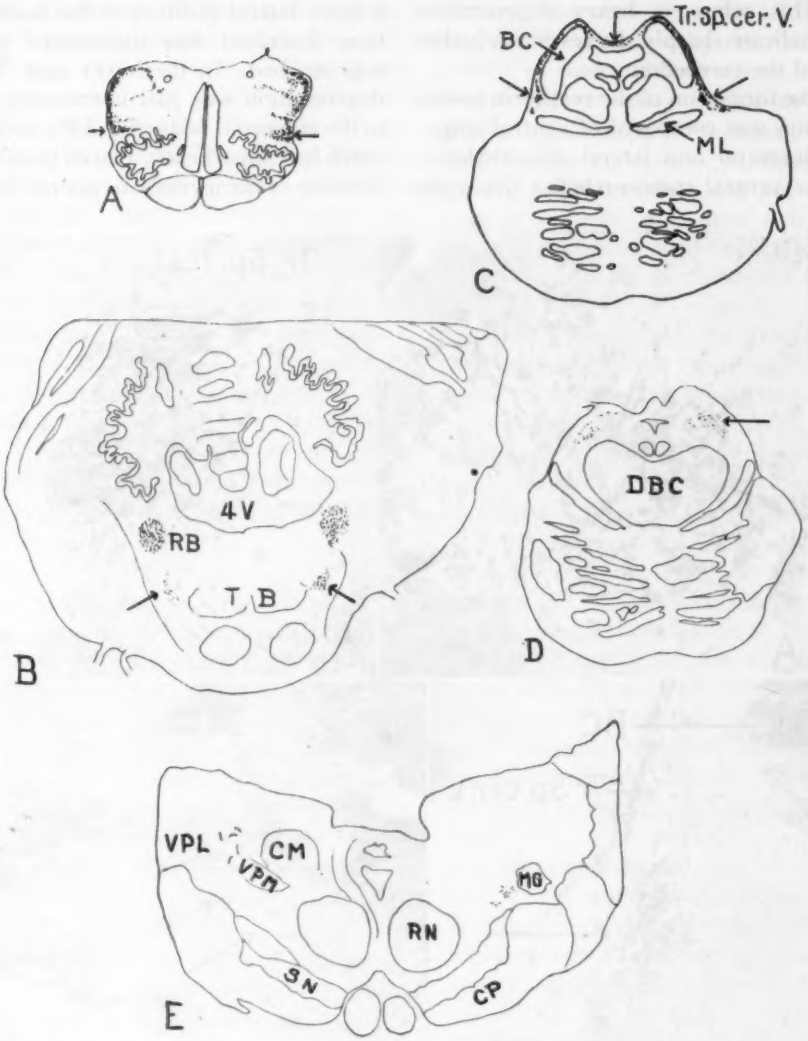

Fig. 3.—Drawings illustrating the course and relative density of degenerating fibers as they ascend in the brain stem; × 1.5 diameters. The specific areas, in addition, are represented in the photomicrographs of figure 4.

A, drawing of a section through the inferior olivary nuclei, illustrating the positions of the lateral spinothalamic tracts (arrows) dorsolateral to the inferior olives. The dorsal spinocerebellar fibers are shifting dorsally into the restiform bodies, and the intermediate positions are occupied mainly by ventral spinocerebellar fibers. This section was also photographed directly (fig. 1 *H*).

B, drawing of a section through the lower part of the pons, indicating the positions of the lateral spinothalamic, spinotectal and ventral spinocerebellar fibers (arrows) dorsolateral to the trapezoid bodies, *T B*. The restiform bodies, containing degenerating dorsal spinocerebellar fibers, lie still more dorsally. *4 V* is the fourth ventricle See figure 4 *A* for photomicrograph of the degenerating fibers.

C, drawing of a section through the upper part of the pons, showing the spinotectal and lateral spinothalamic tracts (arrows) dorsal to the medial lemnisci, *M L*. The ventral spinocerebellar tracts, *Tr. Sp. cer. V.*, are shown entering the anterior medullary velum after shifting dorsally across the brachia conjunctiva, *B C*. See figure 4 *B* for a photomicrograph of the degeneration.

D, drawing of a section through the inferior colliculi, showing the incorporation of the lateral spinothalamic tract into the triangular area at the base of the inferior colliculus (arrow) and the entrance of spinotectal fibers into the inferior colliculus. For a photomicrograph of this area see figure 4 *C*. Decussation of brachia conjunctiva, *D B C*.

E, drawing of a section through the inferior portion of the nucleus ventralis posterolateralis (*V P L*) of the thalamus, indicating the scattered degeneration on each side. This is indicated also in figure 4 *D*. *R N* indicates the red nucleus; *C M*, the centromedian nucleus; *V P M*, the nucleus ventralis posteromedialis; *M G*, the medial geniculate body; *C P*, cerebral peduncles; *S N*, the substantia nigra.

In ascending through the medulla the dorsal spinocerebellar fibers on each side shifted dorsally across the spinal tract of the trigeminal nerve and entered the restiform body (figs. 1 *H* and 3 *A*). This relatively heavy degeneration continued to indicate sharply the restiform bodies as they entered the cerebellum.

Rostral to the formation of the restiform bodies the degeneration was composed of ventral spinocerebellar, spinotectal and lateral spinothalamic fibers, with the ventral spinocerebellar fibers the most superficial. All the fibers occupied a medullary position identical with that described by Schwartz and O'Leary [16] in that they were dorsolateral to the inferior olivary nucleus and extended medially for a distance indicated in figure 3 *A*. This conforms with the observation of these authors that fibers from lower segments occupy a more lateral position in the medulla. The position described was maintained until the pons was reached. In the lower part of the pons the degeneration was just lateral and slightly dorsal to the trapezoid body (fig. 3 *B*), and of course was much less superficially placed than in the medulla. Because of the increase in pontile fibers and nuclei in the upper part of the pons, there occurred a relative shift dorsally in the position of the degenerating fibers, and also of the lateral and

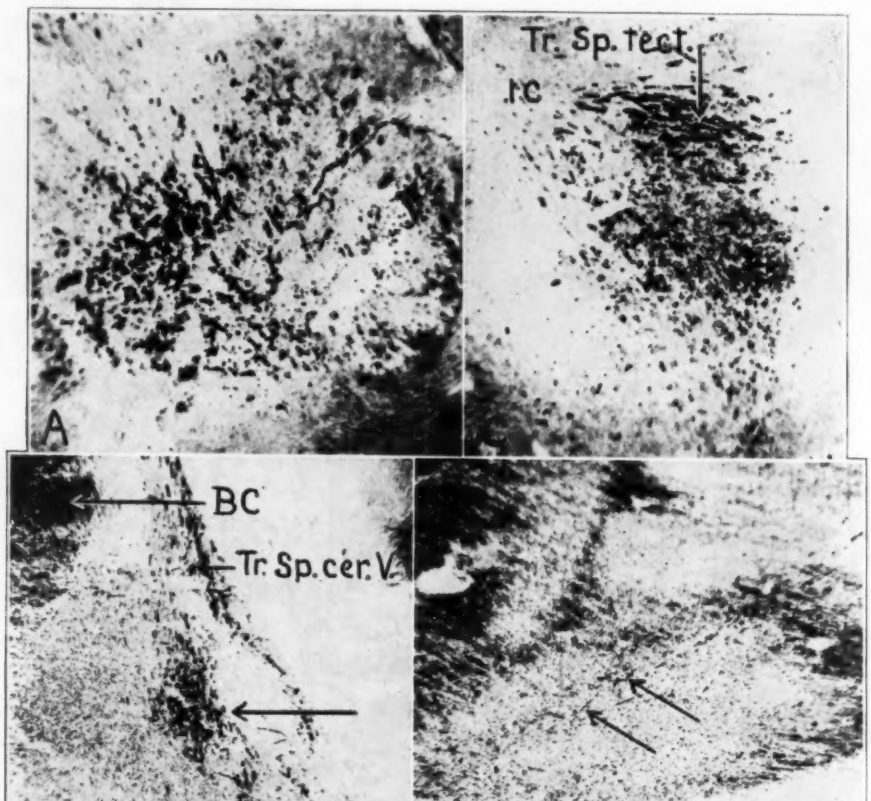

Fig. 4.—Photomicrographs of the areas of degeneration indicated by stippling in figure 3, *B* to *E*. × 20 diameters.

(*A*) The area contains degenerating fibers of the lateral spinothalamic, spinotectal and ventral spinocerebellar tracts (see figure 3 *B*).

(*B*) At this level the lateral spinothalamic and spinotectal fibers (arrow) become incorporated into the base of the lateral lemniscus along the lateral sulcus. Ventral spinocerebellar fibers, *Tr. Sp. cer. V.*, can be seen shifting dorsally across the brachium conjunctivum, *B C*. See figure 3 *C*.

(*C*) Lateral spinothalamic fibers lie at the base of the inferior colliculus (arrow). Spinotectal fibers, *Tr. Sp. tect.*, can be distinguished, since they are oriented transversely as they enter the inferior colliculus, *I C*. See figure 3 *D*.

(*D*) The few degenerating fibers present as the lateral spinothalamic tract enters the thalamus are partially indicated by arrows. See figure 3 *E*.

medial lemnisci. At the level of the anterior medullary velum the degenerating fibers were clearly associated with the lateral lemnisci. Also, at this level ventral spinocerebellar fibers turned dorsally across the surface of the brachium conjunctivum on each side into the anterior medullary velum (figs. 3 *C* and 4 *B*). Rostral to this, only spinotectal and lateral spinothalamic fibers remained. At the level of the inferior colliculi, spinotectal fibers entered the inferior colliculus (figs. 3 *D* and 4 *C*), while the lateral spinothalamic fibers passed through the heavily myelinated triangular area at the base of the colliculus. These fibers ascended in relatively the same position, medial, first to the inferior quadrigeminate brachium and then to the medial geniculate body (fig. 3 *E*) and entered the nucleus ventralis posterolateralis of the thalamus. Fewer degenerating fibers were noted here than at lower levels, but there was no doubt that they ended in this part of the thalamus. Sections above this level revealed no degeneration.

COMMENT

Comparison of the results of the postoperative sensory examinations with the operative levels reveals that after the fibers of the pain pathway enter the cord they cross completely within at least two segments. The incision on the left side of the sixth thoracic segment, for instance, spared fibers derived from the seventh thoracic dermatomal area but included the fibers from the eighth. This, however, gives no indication of the amount of ascent after the first synapse.

The course of the lateral spinothalamic tract as traced with the Marchi technic agrees fairly well with that described by previous observers.[1] The results in this case show that the lateral spinothalamic tract is most easily attacked surgically at its relatively superficial position in the thoracic portion of the cord,[1a] in the medulla [1c] and along the lateral sulcus of the mesencephalon.[6] They also indicate that the usual anterolateral chordotomy interrupts relatively few descending fibers. Some of the degeneration noted below the incisions may have been retrograde, but most of it probably represented degenerating bulbospinal fibers. Anterolateral chordotomy also interrupts part of the dorsal spinocerebellar fibers and probably all of the ventral spinocerebellar fibers, as well as the spinotectal and lateral spinothalamic fibers. The relatively heavy involvement of the dorsal spinocerebellar tract in this case is somewhat surprising. From the extent of the incisions one would expect most of these fibers to be spared. Either the tract extends farther ventrally than is commonly supposed,[2] or postoperative edema in the neighborhood of the incisions affected many of the fibers.

The degeneration throughout the cord was confined to the superficial portions of the lateral funiculi. The incisions did not extend into the anterior funiculi; and since relief was obtained, it is most probable that the lateral spinothalamic fibers ascend only in the lateral funiculi. Hyndman and Van Epps [7] suggested that some of the pain fibers ascend in the anterior funiculi and that because of this incisions must extend into this area, or even to the ventral median fissure. However, their evidence for this assumption is by no means conclusive. They presented Marchi preparations of the spinal cord only in the neighborhood of the incisions, and these showed precipitation of osmic acid in apparently normal areas, which rendered detailed interpretation valueless. Degeneration was present in the anterior funiculi, but this is to be expected, since with these areas cut the ventral spinothalamic tracts will degenerate. The weight of evidence is against a spread as far anterior as this. It must be said, however, that too few detailed examinations and reports are available in the literature to enable one to be dogmatic on this point.

In the cervical portion of the cord the degenerating fibers were more concentrated on the surface and were more dorsally situated, indicating the development of lamination by the entrance and crossing of fibers derived from the cervical and upper thoracic levels. From a comparison of this case with other cases, it is apparent, as other investigators have decided, that there is considerable intermingling of fibers from different levels,[8] so that there is by no means a sharp segmental demarcation within the tract. Because of this it is somewhat difficult to accept the degree of exact topical localization which Hyndman and Van Epps postulated. They stated in their conclusions that with a selected incision analgesia could be confined to the chest. In their one illustrative case, however, analgesia was present over the abdomen, as well as the chest, and initially over the upper portions of the thighs as well.

6. (*a*) Walker, A. E.: Relief of Pain by Mesencephalic Tractotomy, Arch. Neurol. & Psychiat. **48**: 865-880 (Dec.) 1942. (*b*) Dogliotti, A. M.: First Surgical Sections, in Man, of the Lemniscus Lateralis (Pain-Temperature Path) at the Brain Stem, for the Treatment of Diffused Rebellious Pain, Anesth. & Analg. **17**:143-145 (May-June) 1938.

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This observation was, rather, in agreement with the amount of lamination that actually exists in the cord.

The relative lamination present in the medulla is confirmed by comparison of this case and the case of Rasmussen and Peyton [1b] with that of Schwartz and O'Leary.[1c] The last-mentioned authors reported on the total degeneration resulting from an intramedullary tractotomy and by the depths of their incisions showed that fibers from the lower dermatomal areas were more superficially placed. The observations in the present case are in accord with such a conclusion. Also confirming the observations of Dogliotti,[6b] Rasmussen and Peyton,[1b] Schwartz and O'Leary [1c] and Walker [9] is the evidence that in the upper portion of the pons and the lower part of the mesencephalon degeneration is intermingled with fibers of the lateral lemniscus. This and the course of the lateral spinothalamic tract near the base of the inferior colliculus have not yet been adequately described in the current textbooks. There is little evidence that this tract is ever incorporated in the medial lemniscus.

The relative scarcity of degenerating fibers near the thalamus is also confirmed and remains a puzzling feature. In this case, the degenerating fibers arose from the sacral, lumbar and lower thoracic levels and were therefore fewer than would be present after an intramedullary tractotomy. Nevertheless, at their entrance into the thalamus the fibers were few indeed as compared with the numbers seen at lower levels, even when the accompanying tracts are considered. Several explanations may be offered. First, the myelinated fibers composing the lateral spinothalamic tract may be fewer than is to be expected, in which case the bulk of the degeneration seen at lower levels would be due to the involvement of other tracts. If this is the case there is at present no satisfactory method of determining the nonmyelinated component of this tract (fig. 2C). Or the explanation might lie in the transmission by a series of short chains, as postulated by May.[4] Lastly, it is quite possible that near the thalamus many of the fibers lose their myelin and therefore would not exhibit the Marchi reaction. These points should all be considered, but as yet not enough cases have been studied to indicate a definite answer. The number of fibers is enough, however, to establish definitely that they end in the posteroventral part of the thalamus.

9. Walker, A. E.: Somatotopic Localization of Spinothalamic and Secondary Trigeminal Tracts in Mesencephalon, Arch. Neurol. & Psychiat. **48**:884-889 (Dec.) 1942.

SUMMARY

The spinal cord and brain stem of a tabetic patient who died twenty-one days after a bilateral chordotomy were studied with the Marchi technic. The chordotomies were performed at the sixth thoracic segment on the left side and between the fourth and the fifth thoracic segment on the right side. Subjective relief of pains in the legs and gastric crises was obtained, and there was loss of pain and temperature sense up to the sixth thoracic dermatomal area on the left side and to the seventh thoracic dermatome on the right side.

Decussation of the tracts was observed to be completed within two segments, and the degeneration, as shown by the Swank-Davenport modification of the Marchi technic, was almost bilaterally symmetric in ascent. The degeneration included lateral spinothalamic, spinotectal and dorsal and ventral spinocerebellar fibers. Relative lamination was confirmed by the increasingly superficial course of the fibers in the cervical part of the cord and the lower portion of the medulla and their position dorsolateral to the inferior olivary nucleus. Incorporation of the lateral spinothalamic tract into the lateral lemniscus and the area at the base of the inferior colliculus, its entrance into the nucleus ventralis posterolateralis of the thalamus and the relative scarcity of degenerating fibers here were also established.

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ELECTROENCEPHALOGRAPHIC FINDINGS IN CASES OF BROMIDE INTOXICATION

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BOSTON

In 1936 and 1937 Lennox, Gibbs and Gibbs [1] first reported on the effect of bromides and barbiturates on the electroencephalograms of normal persons and of epileptic patients. In normal subjects, the intravenous administration of 5 to 10 grains (0.325 to 0.65 Gm.) of phenobarbital or 30 grains (2 Gm.) of sodium bromide produced no appreciable effect until drowsiness or sleep occurred, at which point the record resembled that obtained during natural drowsiness or sleep. In epileptic patients, on the other hand, a similar dose of either drug tended to shorten and distort the seizure discharges and to prolong the interval between discharges.

Since this early report, a number of investigators have focused their attention on the effect of drugs on the electroencephalogram, emphasis being given to the clinical phenomena accompanying the various phases of intoxication [2] and to the problem of the delirium itself.

In 1938 Rubin and Cohen [3] reported 1 case of bromide intoxication in which a mildly slow pattern (8.3 cycles per second) appeared at a blood bromide level of 59.6 mg. per hundred cubic centimeters, with an appreciable rise in frequency as the level fell to 36.7 mg. per hundred cubic centimeters. None of the slow rhythms characteristic of sleep appeared.

Recently Romano and Engel [4] have studied cases of delirium due to heterogenous disorders, such as cardiac decompensation, malignant hypertension, diabetic acidosis and Brill's disease, and have shown that slow activity is the predominant quality of the electroencephalogram during any of these delirious states, with changes toward normal paralleling clinical improvement. An interesting point was the virtual absence of fast rhythms except those of low voltage, commonly lumped together as "low voltage fast." None of their cases involved delirium due to the bromides.

Progressive slowing of the brain waves has been noted during acute induced alcoholic intoxication,[5] and a mean change in frequency of 2 to 3 cycles per second usually accompanies gross intoxication.[6] In a previous communication, Greenblatt, Levin and di Cori [7] reported a higher incidence of abnormal electroencephalograms for

Miss Marie M. Healey and Miss Helen E. Brennan gave technical assistance.

From the Department of Psychiatry of the Harvard Medical School, and the Boston Psychopathic Hospital.

1. Lennox, W. G.; Gibbs, F. A., and Gibbs, E. L.: Effect on the Electroencephalogram of Drugs and Conditions Which Influence Seizures, Arch. Neurol. & Psychiat. **36**:1236-1250 (Dec.) 1936. Gibbs, F. A.; Gibbs, E. L., and Lennox, W. G.: Effect on the Electroencephalogram of Certain Drugs Which Influence Nervous Activity, Arch. Int. Med. **60**:154-166 (July) 1937.

2. (*a*) Andrews, H. L.: Brain Potentials and Morphine Addiction, Psychosom. Med. **3**:399-409 (Oct.) 1941; (*b*) Changes in the Electroencephalogram During a Cycle of Morphine Addiction, ibid. **5**:143-147 (April) 1943. (*c*) Gibbs, F. A., and Maltby, G. L.: Effect on the Electrical Activity of the Cortex of Certain Depressant and Stimulant Drugs, J. Pharmacol. & Exper. Therap. **78**:1-10 (May) 1943. (*d*) Cohn, R., and Katzenelbogen, S.: Electroencephalographic Changes Induced by Intravenous Sodium Amytal, Proc. Soc. Exper. Biol. & Med. **49**:560-563 (April) 1942. (*e*) Rubin, M. A.; Malamud, W., and Hope, J. M.: Electroencephalogram and Psychological Manifestations in Schizophrenia as Influenced by Drugs, Psychosom. Med. **4**:355-361 (Oct.) 1942. (*f*) Brazier, M. A. B., and Finesinger, J. B.: Action of Barbiturates on the Cerebral Cortex, Arch. Neurol. & Psychiat. **53**:51-58 (Jan.) 1945.

3. Rubin, M. A., and Cohen, L. H.: The Electroencephalogram in Bromide Intoxication, Arch. Neurol. & Psychiat. **40**:922-927 (Nov.) 1938.

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patients suffering from alcoholic psychoses, particularly those characterized by hallucinosis or confusion, than for normal controls or for persons with chronic alcoholism without psychotic manifestations.

The presence of confusion, disorientation and memory impairment (the "organic reaction pattern"), especially in its acute form,[8] greatly increases the probability of finding dysrhythmia in any given case. In our experience the dysrhythmia is often, but not always, of the slow wave type.[9]

The present study deals with the electroencephalograms and the clinical and laboratory findings in a series of cases of bromide intoxication.

Normal and Abnormal Electroencephalograms Encountered at Various Blood Bromide Levels for Patients with Bromidism *

	Under 100 Mg./100 Cc.							100-200 Mg./100 Cc.							Over 200 Mg./100 Cc.						
		Abnormal Electroencephalogram							Abnormal Electroencephalogram							Abnormal Electroencephalogram						
Diagnosis	Normal Electroencephalogram	Fast	Slow and Fast	Slow	Total No. Abnormal	Percentage Abnormal	Total	Normal Electroencephalogram	Fast	Slow and Fast	Slow	Total No. Abnormal	Percentage Abnormal	Total	Normal Electroencephalogram	Fast	Slow and Fast	Slow	Total No. Abnormal	Percentage Abnormal	Total
Bromide psychosis	5	0	0	0	0	0	5	1	1	1	1	3	75	4	2	1	4	6	11	85	13
Bromidism with personality disorders	8	2	1	0	3	27	11	0	0	0	2	2	100	2	0	3	0	1	4	100	4
Totals	13	2	1	0	3	19	16	1	1	1	3	5	83	6	2	4	4	7	15	88	17

* Abnormal electroencephalograms are divided into those with fast, mixed slow and fast and slow activity.

METHODS

Electroencephalographic studies were made with the aid of a Grass six channel, ink-writing oscillograph. Both monopolar and bipolar tracings were taken, and whenever possible a two to three minute record of forced hyperventilation was obtained. Frontal, parietal and occipital leads were applied to both hemispheres, and interconnected leads from the mastoids or the ear lobes served as grounds. Note was made of the patient's condition at the time of the electroencephalographic study, and special attention was paid to the mental picture. Bromide blood levels for these patients were determined by the method of Wuth,[10] usually on the day of the electroencephalographic study, but a few blood bromide values had to be interpolated.

Classification of Electroencephalograms.—The tracings were classified as normal, borderline or abnormal after thorough review of the essential characteristics of each tracing and correction for the age of the patient.[11] In addition, the predominant frequency was determined and classified as follows:

Normal: 8.5 to 12 per second frequency
Fast activity: Predominant frequency above 12 cycles per second
Slow activity: Predominant frequency below 8.5 cycles per second
Mixed fast and slow: A pattern consisting of frequencies both faster and slower than the normal range

The data are both cross sectional and longitudinal. For some patients only one electroencephalogram was taken, and for others several electroencephalograms were obtained over a period. Thus, we observed not only the changes in a single patient during the course of recovery, but the differences between several patients at the same blood bromide level.

PATIENTS

A total of 39 patients referred to the Boston Psychopathic Hospital because of neuropsychiatric disturbances associated with bromide intoxication were studied. Patients with idiopathic epilepsy or known cerebral damage were eliminated from the series.

DATA AND RESULTS

Concerning the relationship between the electroencephalogram and the blood bromide level, the table shows data for the 39 patients with bromide intoxication, divided into two groups: (1) patients (22) with a disorder diagnosed as bromide psychosis; (2) patients (17) having a pronounced personality disorder with bromidism as a secondary feature. For the latter group, of 17 patients, the primary diagnoses were as follows: psychoneurosis, 3 patients; manic-depressive psychosis, 2 patients; dementia precox, 3 patients, and chronic alcoholism, 4 patients.

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9. Greenblatt, M., and Levin, S.: Factors Affecting the Electroencephalogram of Patients with Neurosyphilis, Am. J. Psychiat., to be published.

10. Wuth, O.: Rational Bromide Treatment, J. A. M. A. **88**:2013-2017 (June 25) 1927.

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Percentage of Abnormal Electroencephalograms and Blood Bromide Level.—For the two groups taken together, the percentage of abnormal electroencephalograms increased with the blood bromide level (fig. 1), from 19 per cent, for patients with bromide levels under 100 mg. per hundred cubic centimeters, to 88 per cent, for patients with bromide levels above 200 mg. per hundred cubic centimeters. In the two subgroups the trends are essentially similar. This is entirely in agreement with the clinical observation that the central nervous effects become more marked as the blood bromide level rises. However, it should be pointed out that patients with the same blood bromide level may have entirely different electroencephalograms.

Type of Electroencephalogram and Blood Bromide Level.—In addition to the increased percentage of abnormal electroencephalograms

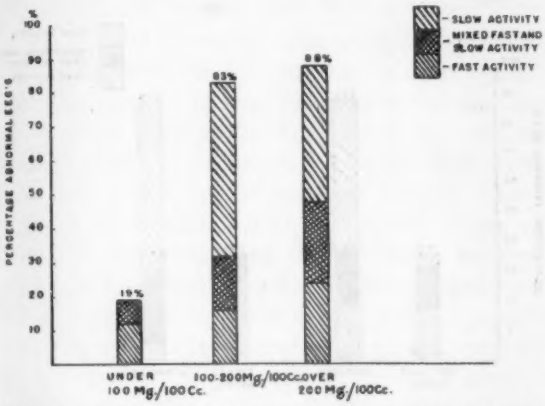

Fig. 1.—Relationship between blood bromide level and percentage of abnormal electroencephalograms. The relative number of electroencephalograms with slow, fast and mixed activity at the various blood bromide levels is also indicated. Read as follows: With 100 mg. of bromide per hundred cubic centimeters of blood, 19 per cent of patients had abnormal electroencephalograms, of which roughly two thirds had fast activity and one third mixed fast and slow activity.

with increased blood bromide levels, there appeared to be, in a number of our cases, a rather characteristic electroencephalographic trend as the blood bromide level rose, or, more strictly (since we studied patients who came to the hospital with high blood levels), as the blood bromide level fell. At high blood bromide levels the electroencephalograms of these patients showed mainly slow activity, the abnormality being diffuse. Irregular, high voltage slow waves in the 2 to 5 per second range were present in the records of 2 patients; the remainder showed frequencies mainly in the 5 to 8 per second range, with occasional slower cycles. In the intermediary ranges of blood bromide concentrations the electroencephalogram tended to show potentials faster than normal, mixed with the slow component, while at low levels of blood bromide the abnormal electroencephalograms usually exhibited abnormally fast activity. When fast activity was present, it was of 12 to 25 per second frequency as a rule and was either intermittent or continuous.

For patients with diffusely slow activity, the average bromide level was 266 mg. per hundred cubic centimeters; for patients with mixed slow and fast activity, 181 mg.; for patients with fast activity, 159 mg., and for patients with normal electroencephalograms, 90 mg., per hundred cubic centimeters.

Two noteworthy exceptions to the general trend of electroencephalographic changes were found. For 1 patient the sequence of events was rather unusual, as shown in the following tabulation:

Time After Entry	Electroencephalographic Type	Bromide Level, Mg./%	Clinical Picture
2 days	Normal 11/sec. activity	239	Confusion; hallucinosis; thick speech
12 days	Normal 11-12/sec. activity	131	Mentally clear; speech normal
24 days	Low voltage 11-14/sec. activity	39	Mentally clear; speech normal
32 days	Medium voltage 11-14/sec. activity with bursts of 18-25/sec. activity	0	Mentally clear; speech normal

This patient had severe chronic alcoholism and had indulged in bromides for one month. Although at the highest blood bromide levels his sensorium was definitely clouded, the electroencephalogram was essentially normal (11 per second rhythm). As the blood bromide level dropped, the electroencephalogram changed only slightly, the principal effect being the introduction of low and medium voltage fast waves in the 11 to 14 per second range. It would seem that the effect of bromide intoxication in this case was to slow a basically fast record to the normal range.

The same phenomenon was noted by Engel and Rosenbaum [6] in cases of acute alcoholic intoxication. When the preintoxication record showed fast or fast normal rhythms, the record during gross intoxication had a frequency distribution within the normal range. In some cases abnormally fast activity became more "normal" during intoxication.

Our other patient, who also had chronic alcoholism, had a normal electroencephalogram at an initial blood bromide level of 360 mg. per

hundred cubic centimeters. On admission this patient presented a picture similar to delirium tremens. A normal electroencephalogram in the presence of severe confusion is unusual.[12] The remarkable resistance to change in the electroencephalogram demonstrated by these 2 patients is an excellent illustration of the extremes of individual variation in response to elevations of the blood bromide.

Relation of Electroencephalogram to Clinical Symptoms.—There was a rather characteristic relationship between the electroencephalographic pattern and the clinical symptoms (fig 2). In general, a clinical picture dominated by confusion and thick speech was associated with an abnormally slow rhythm in the electroencephalogram; improvement in mental clarity and orientation was associated with mixed fast and slow activity, and the later phases of recovery were associated with either mildly fast or normal activity.

Confusion: A total of 17 out of 39 patients were confused, and the majority of these were also hallucinated. Three patients were hallucinated without confusion. (These were the only 3 patients with a diagnosis of dementia precox.) For the patients with confusion and hallucinations, the average blood bromide level was 275 mg. per hundred cubic centimeters; for those with confusion without hallucinations, the average blood bromide level was 224 mg. per hundred cubic centimeters. For 19 patients with clear mentality, the average blood bromide level was 88 mg. per hundred cubic centimeters. The electroencephalographic abnormality for patients with confusion was 88 per cent, as compared with 36 per cent for those without; and the incidence of slow activity was 60 per cent for the patients with confusion, as compared with 12.5 per cent for those without (fig. 2).

Speech Disturbance: Seventeen of the patients displayed evidence of speech disturbance, described variously as "thick speech," "dysarthria" or "slurred speech." Of these, 88 per cent had abnormal electroencephalograms, primarily showing slow activity; and the average blood bromide level for the 17 patients was 245 mg. per hundred cubic centimeters. On the other hand, of the 22 patients with normal speech, only 36 per cent had abnormal electroencephalograms; and the average blood bromide level was 92 mg. per hundred cubic centimeters. The majority of the abnormal records for patients with bromidism but with clear speech exhibited fast activity, and none of the records showed the slow type (fig. 2). All of the patients whose electroencephalograms showed abnormally slow rhythms had some speech disturbance.

Total Protein Content of Cerebrospinal Fluid: Nine patients had examination of the spinal fluid during the period of bromide intoxication. In 5 of these the total protein was elevated (over 45 mg. per hundred cubic centimeters), and in 4 it was within normal limits. No other abnormalities of the cerebrospinal fluid were found except an increased bromide content, which, unfortunately, was inadequately studied. The highest reading for total protein was 108 mg. per hundred cubic centimeters; the lowest was 25 mg. There was a rough correlation of the elevation of total protein in the cerebrospinal fluid, the electroencephalographic abnormality and the

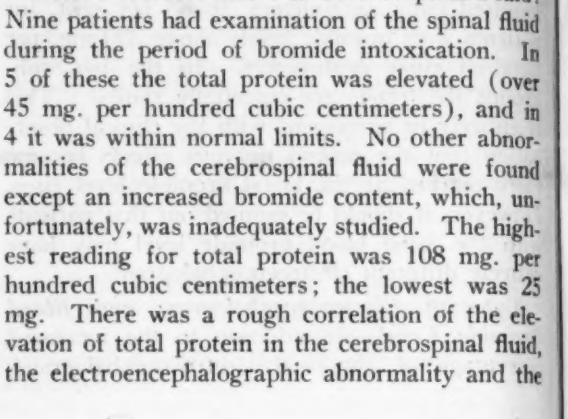

Fig. 2.—Relationship between percentage of abnormal electroencephalograms and clinical symptoms in patients with bromidism. Read as follows: Thirty-six per cent of patients with clear mentality had abnormal electroencephalograms, as compared with 88 per cent of patients with confusion. Approximately one eighth of the mentally clear patients with abnormal electroencephalograms had slow activity, whereas approximately six tenths of confused patients with abnormal electroencephalograms had slow activity.

height of the blood bromide. In 3 cases, spinal punctures were repeated during the course of recovery from bromide intoxication, and in each instance there was a significant drop in the total protein level of the cerebrospinal fluid along with a fall in the blood bromide.

Bromide Rash: Eleven of the patients had bromide rash on entry, whereas 28 were without rash on entry or at any time during the course of recovery. Blood bromide levels varied remarkably both for patients with rash and for those without; readings as high as 380 mg. of bromide per hundred cubic centimeters of blood were

12. Romano and Engel.[4] Greenblatt and others.[7] Greenblatt and Levin.[9]

obtained for persons who were entirely without cutaneous manifestations. The average blood bromide level on admission was essentially no higher for persons with eruption than for those without—229 mg., as compared with 222 mg., per hundred cubic centimeters. Electroencephalographic abnormalities were only slightly more common for persons with rash than for those without (64 per cent, as compared with 57 per cent). The data suggest that the rash is not correlated with either the blood bromide level or the electroencephalogram.

COMMENT

Three important results appear from this investigation of bromide intoxication.

1. There is a clear general trend toward increasing abnormality of the electroencephalogram with rise in the blood bromide level and progressive clouding of the patient's sensorium.

2. There is a definite tendency for the electroencephalograms of the various patients to go through similar phases of recovery—from diffusely slow activity, at high levels of bromide concentration in the blood; through mixed slow and fast activity at intermediate ranges of concentration; to fast activity, at lower ranges of concentration, and, finally, to normal activity, when the bromide is largely or entirely eliminated and the patient returns to normal both physically and mentally. The occurrence of fast activity at intermediary blood bromide levels is similar to the observation of fast activity with moderate intravenous doses of barbiturates, reported by Brazier and Finesinger.[2f] On the other hand, with delirious states not associated with drug factors, Romano and Engel[4] found that fast activity is virtually absent at all stages of the delirious process.

3. There may be remarkable individual variations in the relationship between blood bromide level and electroencephalographic abnormality. Evidently, very high blood bromide levels may at times exist even in the absence of gross electroencephalographic abnormalities. Persons may also differ considerably in the blood bromide level at which the sensorial clearing occurs. Whether the mental picture or the electroencephalogram clears first would seem to be an entirely individual matter; either is possible.

Apart from a fundamental difference in vulnerability of the nerve cell to a toxin such as bromide, other factors may be considered in attempting to account for the striking individual differences in the electroencephalographic findings at the same blood bromide levels:

(*a*) Some patients who have been indulging in bromides for a prolonged period may develop resistance to the drug, or, on the other hand, they may become more sensitive to it.

(*b*) The concentration of bromides in the extracellular fluid bathing the nerve cells may exhibit rapid or marked fluctuations (perhaps associated with the patient's hydration).

(*c*) Individual differences may exist in the effect of bromide on the permeability of the hematoencephalitic barrier. (Not only did an increased protein concentration in the cerebrospinal fluid occur concomitantly with elevation of the blood bromide level, but at the same blood bromide level there was considerable individual variation in the protein level of the cerebrospinal fluid).

Of conceivable clinical significance is the fact that all patients for whom more than one record was taken showed definite changes in the electroencephalographic pattern with time. An abnormal electroencephalogram which exhibits changes toward normal on repetition suggests the possibility of acute organic changes, such as might occur with drug intoxication. It should be borne in mind that both bromide and barbiturate intoxication may be a factor contributing to the high percentage of abnormal electroencephalograms reported in some groups of acutely psychotic patients.

SUMMARY

A study of the electroencephalograms of patients with bromide intoxication reveals the following characteristics:

The incidence of electroencephalographic abnormality is high during the intoxicated state.

A progressive clearing of the patient's sensorium parallels electroencephalographic changes toward normal.

There exists a definite relationship of the blood bromide level, the electroencephalogram and the clinical picture. At high blood bromide levels (over 200 mg. per hundred cubic centimeters) the electroencephalogram tends to show diffuse slow activity, and the patient as a rule is confused and dysarthric. Thus far, no diffusely slow activity has been found in the absence of dysarthria. As the bromide level falls, the electroencephalograms of a number of patients show a phase of mixed slow and fast activity, and

at low levels of bromide concentration the electroencephalogram shows essentially normal or mildly fast rhythms.

The electroencephalogram shows changes over a remarkable range in both frequency and voltage. High voltage activity as slow as 2 cycles per second is occasionally encountered in some of the confused patients with high blood bromide levels. Activity in the 5 to 8 cycles per second slow range is most frequent, however. On the fast side of the frequency spectrum, the activity is of medium or low voltage and is generally in the range of 12 to 25 cycles per second.

A striking phenomenon is the pronounced individual differences in the electroencephalogram and the clinical picture at the same blood bromide level.

74 Fenwood Road (15).

Case Reports

PROGRESSIVE HEMIATROPHY OF THE FACE

MAJOR HAROLD E. SIMON AND LIEUTENANT BERNARD KAYE, MEDICAL CORPS, ARMY OF THE UNITED STATES

Progressive idiopathic hemiatrophy of the face was first described by Romberg in 1846. Since then over 500 cases have been reported, including those analyzed by Archambault and Fromm [1] in 1932, when they reviewed about 400 cases in the literature and reported 3 of their own.

In the case reported by us contralateral hemihypertrophy was present. We are aware of only 1 similar reported case; this was Sterling's, cited by Archambault and Fromm.

REPORT OF A CASE

The patient is a white soldier aged 28 years. His father and mother both died of cancer of the intestinal tract. He had mumps, chickenpox and diphtheria in childhood and measles in 1934. Both shoulders were dislocated and frequent minor injuries of the face were sustained while he was playing football, in 1934-1935. An infection occurred in the left external auditory canal in 1933 and in the upper lip in 1938. He received an honorable discharge from the United States Coast Guard in 1940 because of persistent seasickness, with severe emaciation and weakness, but he recovered completely after his return to civilian life.

Facial asymmetry was first called to his attention in 1938 by friends, and it was then noticed that the condition was apparent in photographs taken about eight years earlier. Just prior to the discovery of the facial atrophy there was aching of the left lower first molar tooth, which was relieved when a cavity was filled. The wasting of the left side of the face progressed until 1943, with resulting loss of strength in the muscles of mastication on that side and limitation of mastication to the right side of the face for the past five years. In recent months a throbbing sensation has been present on the affected side, and for a year frequent cramplike pains, induced by prolonged mastication or by biting on hard objects, have been noted in the right cheek. Occasionally this pain has been accompanied with momentary locking of the jaw, usually when in semiextension. Localized anesthesia, anhidrosis or alopecia has not developed.

The atrophy of the face has not progressed for a year and other areas have not become involved, but moderate progressive enlargement of the opposite side of the face has occurred. Typical migraine headaches, nervousness and increased irritability have been present since 1940. Occasionally fibrillary twitchings and transitory areas of numbness have been present in the legs.

Physical Examination.—The patient was well nourished and well developed. Asymmetry of the face was pronounced (figure): The muscles and subcutaneous tissues of the left side of the face and jaw showed extensive atrophy, involving especially the masseter and, to a lesser extent, the temporal muscle, and a muscle mass was not palpable between the mucous membrane and the skin of the left cheek. The nasolabial fold was less well defined on the left side than on the right. The facial movements were normal, but there existed definite muscular weakness, as shown by inability to hold objects firmly between the upper and lower teeth on the left side. The skin was soft and appeared normal. Pain, tactile and temperature sensations were normal and equal on the two sides of the face, and the cutaneous temperatures of the right and left cheeks were equal. Definite hypertrophy of the opposite side of the face, due largely to increased volume of the masseter muscle, was present. The results of the examination were otherwise normal. Complete ophthalmologic examination revealed nothing abnormal. The left nostril was smaller than the right, but, except for slight deviation of the septum, the intranasal structures were normal. The left ear was larger than the right. The tympanic membranes were normal, and hearing was 20/20 bilaterally. The mouth, pharynx and neck appeared normal. The patellar reflexes were notably decreased; other reflexes were normal. A small area of decreased sensitivity to pain was present in the mesial aspect of the right groin.

Appearance of patient, with atrophy of the left side and hypertrophy of the right side of the face.

Roentgenograms of the skull showed no intracranial abnormality or changes in bone. A periapical abscess of the left lower first molar tooth was apparent. The basal metabolic rate was normal. The Kahn reaction was negative; urinalysis gave normal results, and the dextrose tolerance test was within normal limits. Blood chemistry determinations showed 56 mg. of nonprotein nitrogen, 36.2 mg. of urea nitrogen, 1.6 mg. of creatinine, 208.1 mg. of cholesterol and 11.0 mg. of calcium per hundred cubic centimeters. The erythrocyte, leukocyte and differential counts were normal.

Other than extraction of the abscessed tooth, no treatment was instituted.

1. Archambault, L., and Fromm, N. K.: Progressive Facial Hemiatrophy, Arch. Neurol. & Psychiat. **27**:529-584 (March) 1932.

CLINICAL PICTURE

Facial hemiatrophy has its greatest incidence in the second decade of life, but persons of all ages are susceptible. The onset is insidious, with gradual unilateral loss of substance of the face, usually without subjective symptoms. Typically, the atrophy is limited to one side and may involve any or all of the tissues, including the skin, subcutaneous fat, muscle, bone and cartilage. Involvement of the skin ranges from atrophy to scleroderma-like changes, and anomalies of pigmentation or variations in amount of hair on the involved side may occur. Atrophy of muscle tissue, especially of the masseter and temporal muscles, is present in most cases. Occasionally there is hemiatrophy of the tongue and, in some instances, of the palate. Atrophy of bone is apt to occur only if the onset of the disease occurs at the ages when development of bone is incomplete. Ocular and periocular changes are common and may be evidenced by ptosis, pupillary inequality, narrowing of the palpebral fissure or enophthalmos.

In many of the reported cases involvement of other portions of the body has been present, but the symptoms have presented such a wide variation that it is difficult to reconcile them with a concept of progressive facial hemiatrophy as a distinct clinical entity. It is felt, however, that some of these patients have had typical facial hemiatrophy in the presence of other, unrelated, pathologic conditions, while in others the atrophy of the face has been merely an incident in an entirely different clinical syndrome. There are no laboratory findings of significance.

Little is known concerning the pathologic changes associated with progressive facial hemiatrophy. Archambault and Fromm were able to find only 3 cases in which necropsy was performed; in 2 cases there was proliferative interstitial neuritis in all branches of the trigeminal nerve and in the gasserian and the neighboring ganglia. In the third case no neurologic lesions were found.

The etiologic factors likewise remain obscure. Lesions of the sympathetic nervous system, involvement of the trigeminal nerve or of the diencephalon, polyneuritis, chronic polioencephalitis of unknown origin and endocrine disorders have all been suggested. These theories all lack confirmation and fail to account for the various manifestations presented.

The condition usually becomes static in from one to twelve years, and in uncomplicated cases there is no tendency to serious complications or fatal termination. The value of all suggested treatments is extremely doubtful.

SUMMARY AND COMMENT

The case of progressive facial hemiatrophy associated with contralateral hemihypertrophy presented here is typical in its limitation of atrophy to one side of the face, in contrast to many of the cases reported in the literature in which atrophy of other parts of the body or other abnormalities coexisted. The associated hypertrophy of the opposite side of the face is a condition found in only 1 of the cases encountered in the literature. It may be physiologic, compensating for the weakness of the involved side and made possible by the strict unilaterality of the process and the otherwise normal, active condition of the patient.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Psychiatry and Psychopathology

PSYCHOMOTILITY IN BEHAVIOUR DISORDERS AS SEEN IN THE HANDWRITING OF CHILDREN. SELNA SCHRYVER, J. Nerv. & Ment. Dis. **100**:64 (July) 1944.

The study of a subject's handwriting gives a clue to his psychomotility, and through this, information as to his personality makeup can be obtained. With children the study of handwriting is handicapped by the subject's difficulty in spelling and by lack of routine. To overcome this the author has worked out a test in which children are asked to write a number of simple basic parts of the usual letters at least twenty times each. In a series of 100 specimens of handwriting written by a group of children with various psychiatric disorders there were indications of the intelligence level, character traits and emotional maturity of the writer. Aggressive, noisy children produced samples marked by great pressure and angularity, while preoccupied children with feelings of inferiority had small letters characterized by short endings, low pressure and hesitating beginnings. Psychotic children showed splitting of forms, exaggeration of size and contraction and alteration of forms. In evaluation of the samples, the gestalt, as well as other details, must be considered for a rounded picture.

CHODOFF, Langley Field, Va.

Meninges and Blood Vessels

MENINGOCOCCIC INFECTIONS: REPORT OF 43 CASES OF MENINGOCOCCIC MENINGITIS AND 8 CASES OF MENINGOCOCCEMIA. H. WEBSTER SMITH, LEWIS THOMAS, JOHN H. DINGLE and MAXWELL FINLAND, Ann. Int. Med. **20**:12 (Jan.) 1944.

Smith, Thomas, Dingle and Finland report on 51 patients with meningococcic infections admitted to the Boston City Hospital in the two year period beginning Sept. 1, 1940. Included among the 51 patients were 43 with meningitis and 8 with meningococcemia without clinical evidence of meningitis. The study was made in order to emphasize some of the less commonly recognized features of the clinical course, the laboratory findings and the therapy of meningococcic infections.

The authors noted from their case studies that one or more of the commoner findings of meningococcic meningitis may be absent in a given case. It was possible to make a tentative diagnosis of meningococcic meningitis in almost every instance by examination of a smear of the cerebrospinal fluid or its sediment stained with Gram's method. However, the group II meningococcus should be carefully distinguished from the gonococcus, especially in cases in which the organism is recovered only from the blood.

The initial dose of a sulfonamide drug should be administered intravenously to patients with meningitis even if they appear only moderately ill when first seen. All but 2 of the patients with meningitis who recovered showed objective signs of clinical improvement twenty-four hours or less after sulfonamide therapy.

The authors state that patients with a relative bradycardia, even though they may appear only moderately ill, should be observed for evidence of increased intracranial pressure. Lumbar puncture is of diagnostic value and should be employed as a therapeutic measure for the symptomatic relief of increased intracranial pressure. The presence of a normal sugar content of the cerebrospinal fluid following sulfonamide therapy or parenteral administration of dextrose was found to be, in itself, of no value in estimating the patient's clinical status. Pulmonary involvement was frequent in the patients with meningococcic meningitis and probably represented a local infection with the meningococcus, either alone or in association with other organisms.

There were 9 deaths among the 43 patients with meningococcic meningitis, but there were no fatalities among the 8 patients with meningococcemia.

GUTTMAN, Philadelphia.

SOME CLINICAL ASPECTS OF MENINGOCOCCIC INFECTION. F. DENNETTE ADAMS, Ann. Int. Med. **20**:33 (Jan.) 1944.

Adams discusses some of the less known or more frequently forgotten manifestations of meningococcic infection. Meningococcemia with acute meningitis, acute fulminating meningococcic septicemia (Waterhouse-Friderichsen syndrome), meningococcemia with arthritis and chronic meningococcemia are briefly considered. Meningitis may occur in any case which belongs in one of the last three groups, but the diagnosis must and can be made in the absence of symptoms and signs of meningeal involvement.

The author states that the response to sulfonamide drugs is little short of miraculous. Sulfadiazine at present is regarded as the drug of choice, with sulfathiazole a close second. He stresses the value of prompt and adequate sulfonamide therapy, the first dose being given intravenously. The condition of the patient is deemed the best guide to subsequent sulfonamide therapy. An adequate fluid intake is essential. Adams advises the use of meningococcus antitoxin for all patients who appear to be severely ill. Also, adrenal cortex extract and blood plasma may tide the patient over a period of so-called circulatory collapse.

GUTTMAN, Philadelphia.

THE MECHANISM AND TREATMENT OF RAYNAUD'S DISEASE. ISIDOR MUFSON, Ann. Int. Med. **20**:228 (Feb.) 1944.

Mufson reports 6 cases of Raynaud's disease. His observations led him to state that there exists a causal relationship between the chief somatic complaint and both the personality derangement and the emotional disturbance. Cooling of the skin is the trigger mechanism which renders complete the partial occlusion of the minute vessels, which has been initiated and is sustained by personality and social-economic derangements. It is further postulated that this cyclic type of vasospasm induces a nonspecific endarteritis, with secondary spasm and endovascular thrombi. Repeated insults of this type lead to chronic tissue hypoxia.

Mufson concludes that only a combination of therapeutic measures directed, first, toward improvement in mental hygiene and alleviation of social-economic derangements, and, second, to an increase in collateral circulation will obtain a total cure of all degrees of severity of Raynaud's disease.

GUTTMAN, Philadelphia.

TEMPORAL ARTERITIS: A LOCAL MANIFESTATION OF A SYSTEMIC DISEASE. JULIUS CHASNOFF and JEFFERSON J. VORZIMER, Ann. Int. Med. **20**:327 (Feb.) 1944.

Chasnoff and Vorzimer report the case of a patient who had arteritis of the temporal vessels. Necropsy revealed evidence of a generalized systemic arterial disease. The authors conclude that arteritis of the temporal vessels is a common local manifestation of a systemic arterial disease which must no longer be regarded as benign.

GUTTMAN, Philadelphia.

RECURRENT PNEUMOCOCCIC MENINGITIS TREATED WITH SULFONAMIDES. HENRY HOPKINS, L. C. HATCH, H. P. SCHENCK and D. S. PEPPER, Ann. Int. Med. **20**:333 (Feb.) 1944.

The authors report a case in which meningitis developed during the course of a sinusitis which was subsequently treated surgically. Type XVIII pneumococcus was isolated. The meningitis apparently subsided after administration of sulfapyridine and antipneumococcic serum. The patient experienced two more episodes of meningitis. Over a period of about thirteen weeks, 182 Gm. of sulfapyridine, 180 Gm. of sulfathiazole and 1,600,000 units of antipneumococcic serum were administered. Recovery was apparently complete.

GUTTMAN, Philadelphia.

BIOLOGIC FALSE POSITIVE SPINAL FLUID WASSERMANN REACTIONS ASSOCIATED WITH MENINGITIS. VIRGIL SCOTT, FRANK W. REYNOLDS and CHARLES F. MOHR, Am. J. Syph., Gonor. & Ven. Dis. **28**:431 (July) 1944.

Scott, Reynolds and Mohr report 7 cases of confirmed false positive reactions of the spinal fluid of nonsyphilitic persons during the course of meningitis. In 3 cases the meningitis was of tuberculous, in 2 of meningococcic, and in 2 of aseptic lymphocytic type. An additional case is included in which transfer of reagin from the blood to the spinal fluid may have occurred during an illness characterized by aseptic lymphocytic meningitis. These cases were from a series of 271 cases of meningitis of one of the types mentioned.

Unconfirmed positive Wassermann reactions of the spinal fluid were observed in an additional 20 cases of various types of acute intracranial disease occurring in nonsyphilitic patients. These cases were from a series of 200 cases of such diseases as pneumococcic, influenzal, streptococcic and staphylococcic meningitis; poliomyelitis; subarachnoid hemorrhage, and tumor of the cerebellopontile angle. The authors state that the positive Wassermann reactions could have been due to a technical error.

These observations indicate that in view of the occurrence of false positive Wassermann reactions of the spinal fluid, the diagnosis of neurosyphilis, based solely on the Wassermann reaction, is unjustified in cases of meningitis and other types of acute intracranial processes until repeated tests performed after the condition has completely subsided demonstrate the continued presence of reagin. False reactions are usually short lived, for in 7 of the 8 cases reported in this series the reaction was transitory.

GUTTMAN, Philadelphia.

Diseases of the Brain

THE CLINICAL ASPECTS OF TRAUMATIC EPILEPSY. D. DENNY-BROWN, Am. J. Psychiat. **100**:585 (March) 1944.

Denny-Brown, in reviewing the status of traumatic epilepsy, states that for this purpose head injury should be defined as injury to the skull which might directly or indirectly cause damage to the brain. Gunshot wounds resulting in penetration of the dura are twice as likely to produce epilepsy as are those which penetrate only the scalp and bone. Scalp wounds due to missiles produce epilepsy more readily than similar wounds caused by blunt instruments. The high liability to epilepsy is therefore inherent in localized injury to the brain; this is in contrast to concussion, which is a generalized cerebral disturbance. The incidence of traumatic epilepsy is much lower in civilian than in military practice. While some confusion exists in the literature regarding the importance of foreign bodies within the cerebrum, it appears that in themselves they do not materially increase the tendency to seizures. Wound sepsis, however, operates strongly in favor of the development of seizures. The duration of posttraumatic amnesia is an indication only of generalized cerebral disturbance and is not related to the development of seizures. The average time interval between the head injury and the first seizure is over two years, with extremes as great as twenty years. Denny-Brown states there is a common association of quasifugue states and traumatic epilepsy. A personality change, usually not clearcut, toward impulsive, irritable, reckless behavior may herald the appearance of epilepsy. Minor attacks, commonly preceded by a vertiginous aura, may be a precursor of traumatic epilepsy. Denny-Brown believes that neither the immediate nor the later electroencephalographic changes associated with head injury and seizures can be related to the presence of hereditary epilepsy. He indicates that not all epileptogenic scars are cerebrodural and that some are not fibrous. Jacksonian attacks or seizures with focal onset occur in less than one-half the cases of traumatic epilepsy, and localized jacksonian epilepsy has an excellent prognosis for surgical treatment.

FORSTER, Philadelphia.

THE ELECTROENCEPHALOGRAM IN POST-TRAUMATIC EPILEPSY. FREDERIC A. GIBBS, WALTER R. WEGNER and E. L. GIBBS, Am. J. Psychiat. **100**:738 (May) 1944.

Gibbs, Wegner and Gibbs point out that the amount of abnormality present in the electroencephalogram after head injury depends on the physical force applied to the brain, the ability of the brain to withstand the blow and the time that has elapsed after the injury. They divided their material into cases of mild and cases of severe head injury and studied it in relation to the importance of age and the time interval after injury. They studied 175 cases of post-traumatic epilepsy and 215 cases of head injury without convulsions. The latter group was further divided into cases of mild and cases of severe head injury. In all cases electro-

encephalograms were taken three or more months after the injury, so that only the chronic post-traumatic state was considered. The records of the three groups of post-traumatic patients were compared with the records of 1,161 epileptic patients and of 1,000 normal control subjects.

In patients with severe head injuries but without seizures the incidence of abnormalities in the electro-encephalograms continued to decrease from three months to two years after injury, while within the same time limits there was a slight decrease in abnormalities in the records of patients with post-traumatic epilepsy. Mild head injuries were found to increase but slightly the incidence of abnormalities over that found for the control group, whereas with severe head injuries the incidence of abnormalities was more than twice that for the control group. After head injury, children were more likely than adults to have abnormalities in the electroencephalogram, and they showed a greater tendency to focal abnormalities. Focal abnormalities of the electroencephalogram were four times as common for patients with post-traumatic epilepsy as they were for unselected epileptic patients. Their appearance correlated well with the occurrence of focal seizures and strongly suggested focal damage to the brain.

The incidence of focal disturbances of the electroencephalogram for patients with post-traumatic epilepsy was twenty-one times that for patients with head injury without seizures.

Gibbs, Wegner and Gibbs state that subjective complaints after head injury cannot be correlated with electroencephalographic abnormalities and that a normal electroencephalogram does not exclude the possibility of cerebral damage or post-traumatic epilepsy. They give a detailed statistical evaluation of the presence of normal and abnormal patients, both focal and generalized, in the electroencephalogram after head injury.

FORSTER, Philadelphia.

ENCEPHALOPATHY, NEPHROSIS, AND RENAL GRANULOMA FOLLOWING SULFONAMIDE THERAPY. BERNARD MAISEL, CHARLES S. KUBIK and JAMES B. AYER, Ann. Int. Med. **20**:311 (Feb.) 1944.

Maisel, Kubik and Ayer report a case in which the outstanding symptom was somnolence to the point of stupor. The patient was very sensitive to mushrooms, and on several occasions mushoom soup was followed by nausea and loss of consciousness. The current disturbance in the state of consciousness followed a twenty-four day period of oral administration of sulfonamide compounds (sulfathiazole 24 Gm., sulfadiazine 6.5 Gm. and sulfanilamide 2 Gm.). The chemotherapy was employed after the removal of a ureteral calculus. The patient died quietly thirty-six days after the initial dose of sulfathiazole. At no time were any significant neurologic signs noted.

At necropsy diffuse cerebral and cerebellar changes were observed. In spite of the lack of clinical evidence of renal impairment, the parenchymal and vascular changes were similar to those produced in experimental studies on the sulfonamide drugs.

The authors conclude that, though some of the cerebral and cerebellar changes observed were similar to those seen in patients whose death was preceded by various severe illnesses, the presence of renal changes characteristic of sulfonamide intoxication suggested that the cerebral and cerebellar changes resulted from sulfonamide therapy.

GUTTMAN, Philadelphia.

BACTEROIDES INFECTIONS OF THE CENTRAL NERVOUS SYSTEM. WILLIAM E. SMITH, ROBERT E. MCCALL and THOMAS J. BLAKE, Ann. Int. Med. **20**:920 (June) 1944.

Smith, McCall and Blake report 4 cases of infection of the central nervous system with an organism of the bacteroides group. In 2 cases meningitis and in 2 cerebral abscess was present. The authors found data in the literature on 11 fatal cases of infection of the central nervous system with Bacteroides.

Infection of the central nervous system due to Bacteroides arises most commonly from chronic otitis media, usually associated with mastoiditis. It is more frequent in adults, and its symptoms correspond to those associated with other pyogenic infections of the central nervous system. The onset of Bacteroides meningitis is acute, with elevation of temperature, headache and stiffness of the neck. The onset of cerebral abscess due to an organism of this group is less acute and may be signalized only by headache and vomiting. In cases of cerebral abscess, the cerebrospinal fluid may be clear. In cases of meningitis, the fluid is cloudy; the cell count ranges from 2,000 to 45,000 cells per cubic millimeter, and the sugar content is decreased, but the protein content is increased. The diagnosis depends on cultivation of the organisms—anaerobic, gram-negative, non-spore-bearing bacilli. Anaerobic cultures should be made in cases of meningitis or cerebral abscess, especially of otitic origin, when gram-negative bacilli are seen in smears or when no organisms can be cultivated aerobically. Primary isolation of bacteroides is greatly facilitated by addition of 30 per cent ascitic fluid to the medium. The course may be acute, with death occurring between the fourth and the ninth day in fatal cases. Recovery, when it occurs, may be prompt or prolonged, depending on the severity of the meningitis and the presence or absence of cerebral abscess.

On the basis of the cases already reported in the literature, the prognosis appears hopeless. However, 3 of the authors' 4 patients recovered. The authors state that the three factors which may have aided in recovery were more adequate surgical and supportive treatment and sulfonamide therapy. The treatment of choice, at present, consists of early and adequate surgical procedures to remove foci of infection in the ear and mastoid; repeated lumbar punctures for drainage of fluid, in cases of meningitis; appropriate measures for drainage of cerebral abscess; attention to indications for intravenous administration of fluids and transfusions, and sulfadiazine therapy.

GUTTMAN, Philadelphia.

MÉNIÈRE'S DISEASE. J. R. LINDSAY, Arch. Otolaryng. **39**:313 (April) 1944.

Lindsay examined the temporal bones of a middle-aged man who had had Ménière's disease for three years. During an attack of vertigo he fell, sustained a fracture of the skull and died of subdural hematoma. The temporal bones were fixed in a solution of formaldehyde and prepared in the usual way. The left bone was serially sectioned in the vertical plane, and the right bone was sectioned horizontally. The pathologic changes in the right ear were limited to the vascular congestion and hemorrhage in the modiolus and to the degenerative changes in the spiral ganglion. The former were due probably to the cranial trauma, while the changes in the ganglion were thought to be related directly to the hearing loss for tones above the frequency of 2048 cycles.

On the left side, the membranes of the internal ear were well preserved. The cochlear duct was greatly dilated, and beginning herniation of the duct through the helicotrema was observed. There was degeneration of cells of the spiral ganglion in the basal coil. The ductus reuniens was of normal size. The saccule almost completely filled the vestibule, and the wall of the saccule overlay the stapedial foot plate. The utricle was dilated in the lower portion leading to the ampulla of the posterior canal, where a tendency to herniate behind the thick wall of the ampulla was seen. The walls of the semicircular canals were normal.

The cause of the hydrops was not evident on histologic examination.

RYAN, M. C., A. U. S.

HEMANGIOBLASTOMA OF THE MEDULLA (LINDAU'S DISEASE). MERVYN H. HIRSCHFIELD, J. Nerv. & Ment. Dis. **99**:656 (May) 1944.

Lindau's disease is characterized by retinal angiomatosis and by hemangioblastomas of the cerebellum, brain stem and spinal cord, with cyst formation and syringomyelia. Cystic areas occur in the pancreas, kidneys and liver. Hirschfield reports the case of a man aged 21 with von Hippel's disease in whom signs and symptoms of medullary involvement developed. He was treated with radiation, receiving a total of 1,475 r in twenty-six days, with remarkable improvement in the neurologic signs.

CHODOFF, Langley Field, Va.

CENTRAL NERVOUS SYSTEM COMPLICATIONS ARISING FROM DISEASES OF THE BLOOD FORMING TISSUES. STACY R. METTIER, J. Nerv. & Ment. Dis. **99**:758 (May) 1944.

Mettier reviews the clinical manifestations referable to the central nervous system in a large series of cases of various diseases of the blood-forming tissues. In treatment of the neurologic aspects of pernicious anemia, early and vigorous liver therapy is essential, and it will produce considerable improvement in three to six months. Certain malignant neoplastic processes involving the hematopoietic structures may give rise to pressure symptoms within the central nervous system. Of these, Hodgkin's disease and lymphosarcoma are the most important, with an incidence of neurologic complications, of various sorts, of 10 to 14 per cent. In 20.5 per cent of a series of 334 cases of leukemia neurologic symptoms were present. The author has seen several instances of a Ménière type of vertigo due to leukemia. Diseases characterized by hemorrhagic diathesis may be marked by subarachnoid or intracerebral hemorrhage. Four cases of this type were observed with thrombocytopenic purpura. Severe anemia due to rapid loss of blood may be complicated by focal convulsions, due either to the fall in blood pressure or to the irritating effects of anoxemia on the cortical cells.

CHODOFF, Langley Field, Va.

Vegetative and Endocrine Systems

THE MORGAGNI-STEWART-MOREL SYNDROME: REPORT OF A CASE WITH PNEUMOENCEPHALOGRAPHIC FINDINGS. MATTHEW T. MOORE, Arch. Int. Med. **73**:7 (Jan.) 1944.

Moore reports the case of a 39 year old woman whose difficulties consisted of seizures, double vision, headaches, periods of disturbance in gait and clumsiness and, perhaps, a mild menstrual abnormality. During the patient's hospitalization it was reported that the mood varied from depression to euphoria. There were no gross abnormal neurologic signs. Roentgenograms of the skull revealed a thickened calvaria, with frontoparietal hyperostosis frontalis interna and calcification in the falx. Pneumoencephalographic examination revealed pronounced cortical atrophy over the frontal and parietal lobes, atrophy of the islands of Reil and moderately advanced internal hydrocephalus, with asymmetry and irregularity of the lateral ventricles.

The condition is regarded as the Morgagni-Stewart-Morel syndrome.

GUTTMAN, Philadelphia.

ADRENAL CORTICAL FUNCTION INDEPENDENT OF DIRECT NERVOUS ACTION: A NEUROLOGICAL STUDY OF NORMAL, DENERVATED AND TRANSPLANTED ADRENAL GLANDS OF ALBINO RATS. W. E. MACFARLAND, J. Exper. Zool. **95**:345 (April) 1944.

In 10 animals, wallerian degeneration within the adrenal gland after excision of the greater and lesser splanchnic nerves produced marked changes in the medulla but no detectable cytologic changes in the cortex.

In 48 animals, the left adrenal was transplanted to the left inguinal region. The animals were divided into two groups. In 8 rats of one series, the transplant was recovered as a small nodule of cortical tissue. In the other 24 rats the right adrenal was removed five to three hundred and seven days after transplantation of the left adrenal. Fifteen of these animals died from one to fifteen days after the operation, and the transplants were removed from the 9 survivors from six to forty-two days after loss of the right adrenal gland.

The functional activity of the transplants was shown by the survival of the animals and by their changes in weight after each operation. Bilateral adrenalectomy in rats of this stock produced death in one to seventeen days.

Microscopic examination of serial sections of normal adrenal glands showed a few small bundles and scattered fibers of nerves passing, without branching, through the cortex to terminate in the medulla. Examination of functional transplants showed robust masses of cortical tissue which were lacking in medulla or any detectable nerve content.

Regeneration was most effective when (*a*) the whole left adrenal was transplanted and (*b*) the right adrenal gland was left in situ for not longer than ten days before removal. About 69 per cent of the glands transplanted in toto showed functional regeneration.

Ganglion cells were not noted in the cortex but were observed in the medulla in about 50 per cent of all the adrenals examined. Ganglion cells may be more abundant in the right than in the left adrenal gland. All the evidence indicates that the medulla of the adrenal gland is the only part which is innervated by secretory fibers and that there is no direct neural control of the functional activity of the cortex.

REID, Boston.

RETURN OF VIRILITY AFTER PREFRONTAL LEUCOTOMY, WITH ENLARGEMENT OF GONADS. R. H. HEMPHILL, Lancet **2**:345 (Sept. 9) 1944.

Hemphill reports the case of a man aged 33 with an obsessional neurosis, which had increased in severity since the first symptoms appeared, at the age of 23. He had been sexually potent but had lost his libido and became impotent at the age of 28. He had lost weight, owing to a highly inadequate intake of food. His testes were tiny and soft on admission, and the penis was thin and long. There was little hair on the body, and it

was falling out on the pubis. Biopsy of the testes showed shrunken tubules, hyalinization of the basement membrane, loss of seminiferous epithelium, absence of mature sperm forms and no compensatory hyperplasja of interstitial cells. Excretion of 17-ketosteroids was 3.8 mg. per twenty-four hours. Protracted attempts to increase his weight failed, and eighteen months later a prefrontal leukotomy was performed. The day after operation his appetite showed great improvement, and he gained weight rapidly. His penis became longer and thicker; the testes became large and firm and descended noticeably, and the scrotum developed to accommodate them. All his obsessions disappeared, and he became good natured and complacent, though a bit lazy. Four months after operation he had normal libido and potentia. The output of 17-ketosteroids rose to 8.87 mg. per twenty-four hours. He married and held a position as a clerk.

Since the weight and atrophy of the genitalia had remained unchanged for years prior to operation, in spite of other therapy, Hemphill feels certain that the change can be attributed entirely to the surgical procedure. He states that perhaps frontohypothalamic, as well as thalamic, pathways were interrupted, thus serving to release pituitary inhibition of the gonads.

McCarter, Boston.

Treatment, Neurosurgery

Surgical Management of Compound Depressed Fracture of Frontal Sinus, Cerebrospinal Rhinorrhea and Pneumocephalus. E. S. Gurdjian and J. E. Webster, Arch. Otolaryng. **39**:287 (April) 1944.

Over a twelve year period (1930-1942) Gurdjian and Webster treated 31 patients with compound depressed fracture of the frontal sinus and in its neighborhood, 9 with cerebrospinal rhinorrhea and 9 with pneumocephalus.

Compound depressed fracture of the frontal sinus and its neighborhood may establish a communication between the nose and the cranial cavity. Hence, it is a potential source of infection, and the rationale of operative intervention is to repair the communication between the intracranial cavity and the nasal spaces and thus to obviate the possible contamination of the former.

Automobile accidents rank far ahead of other sources of trauma in producing compound depressed fractures in this region. The fractures of about 75 per cent of the 31 patients were due to motor accidents. Seven patients in the group were not rendered unconscious at the time of their injury; 13 gave a history of a short period of unconsciousness, and 11 had evidence of severe damage to the brain. Twenty-one patients in the group had dural tears, varying from small punctures to extensive lacerations. In fully one half of these persons there was underlying lacerated and necrotic brain tissue. Cerebrospinal rhinorrhea occurred in 4 patients, and pneumocephalus was observed in 3 patients. Meningitis developed in 3 patients, 2 of whom recovered. Brain abscess occurred in 1 patient and was successfully treated. Three of the group of 31 patients died, 2 as a result of associated damage to the brain and 1 as a result of meningitis.

Compound depressed fracture in the region of the frontal sinus should receive surgical treatment as soon as the condition of the patient permits. Careful roentgenographic examination should precede every operative repair, so that the extent of bony damage may be carefully evaluated before operation. The authors prefer exposing the lesion by extending the initial laceration in an appropriate manner. In some cases a fronto-temporal skin flap is made. The comminuted pieces of bone are removed from the outer wall of the frontal sinus. The interior of this sinus is then carefully inspected, and comminuted and depressed pieces, if present, are removed. Dural tears are repaired with silk. If the necrotic brain tissue is found in the sinus, it is sucked away. If the tear in the dura is beyond repair, the edges are approximated and held together with sutures, and the area is packed with antiseptic gauze to hold the dura away from bony attachments. The pack may be removed slowly over a period of six to eight days, or the wound may be closed completely and six to eight days later reopened for removal of the pack. In the absence of local infection, repair of the bony defect may be undertaken four to six months after the accident. If postoperative infection occurs, the defect may be repaired eight to ten months after the infection has completely cleared up. In repairing the defect, osteoperiosteal transplants or a plastic substance called "plexiglas" may be employed.

Traumatic cerebrospinal rhinorrhea is a serious complication of head injury, even with the availability of chemotherapeutic drugs. It is probably more common than is observed or described, as the leakage may not be detected because of the patient's prone position in bed. The condition is serious because infection may enter the cranial cavity from the nasal passages. Meningitis and cerebral abscess are common sequelae. Healing of acute cerebrospinal rhinorrhea, with no reappearance of leakage, may take place during absolute rest in bed. When it recurs on one or more occasions, closure of the fistulous tract without operative intervention is rare, and meningitis or abscess of the brain or both may develop months or even years after the accident. In such cases treatment is difficult, and frequently death results.

Of the 13 patients reported, 8 were seen in the acute stage of trauma to the head, and 5 had recurrent cerebrospinal rhinorrhea. Of the patients seen during the acute phase, 4 had surgical treatment, and the remaining 4 were treated conservatively. The indication for operation on 3 patients was the presence of a compound depressed fracture of the frontal sinus and in its neighborhood. The other patient receiving surgical treatment had a comminuted fracture of the inner wall of the frontal sinus and of the cribriform plate, with no laceration of the forehead. Treatment may be conservative or operative or both. If a conservative measure is decided on, the patient is strictly confined to bed and is given prophylactic doses of sulfonamide compounds. If operative management is desirable, the problem varies according to the type of condition. In a case of compound depressed fracture, the initial wound may be enlarged by appropriate extension, the area of damage exposed and the torn dura repaired. In a case of recurrent rhinorrhea with no complications, the anterior fossa may be exposed by turning a low frontal flap. The torn dura is then exposed externally and repaired. When a complicating condition is already present, treatment is directed first to the complication, before repair of the cranionasal fistula is considered.

Pneumocephalus may be present without cerebrospinal rhinorrhea, and many patients with cerebrospinal rhinorrhea have no associated pneumocephalus. The usual avenue of entrance of air is a cranionasal fistula. Fracture through the petrous bone is the second avenue of entrance, with bloody or cerebrospinal otorrhea as a sequela. In 4 patients in this group, pneumocephalus was associated with cerebrospinal rhinorrhea, and in

4 others, with cerebrospinal or bloody otorrhea. In 1 patient a compound depressed fracture of the occipital region which had been left untreated for five days was the avenue of entrance of air. The air may be subdural, ventricular, intracerebral or subarachnoid. Most commonly it is subdural, while subarachnoid accumulation is rare. Diagnosis is simple after roentgenographic examination.

Conservative treatment, namely, strict rest in bed in a semi-Fowler position, has a definite place in the management of pneumocephalus associated with acute injury of the head. For the acute form of pneumocephalus, operative intervention may be indicated because of the presence of compound depressed fracture in the neighborhood of the frontal sinus or elsewhere. Pneumocephalus appearing months or years after the acute injury is treated surgically. Usually latent pneumocephalus is due to a cranionasal fistula. If the fistula extends through the anterior fossa, an adequate frontal bone flap may be used to explore the region extradurally and intradurally.

RYAN, M.C., A.U.S.

REPAIR OF PERIPHERAL INJURIES OF THE FACIAL NERVE. R. C. MARTIN, J. Nerv. & Ment. Dis. **99**:755 (May) 1944.

Early attempts at repair of the peripherally injured facial nerve utilized the hypoglossal and spinal accessory nerves for the proximal segments and the facial nerve for the distal portion. If no proximal segment of the facial nerve can be found, this operation is useful, although distressing associated movements occur. Bunnell, in 1927, performed a successful end to end suture of the facial nerve by removing the intratympanic portion of the nerve from its bed and shifting it anteriorly. Homologous sensory or motor grafts have been used as bridges by which the axons gain access to the distal facial trunk. End results in patients treated by these methods show no contractures, but there remain associated movements when strong volitional movements are attempted. Function of the frontalis muscle is seldom regained.

CHODOFF, Langley Field, Va.

PREVENTION OF FATALITY AND FRACTURE DURING ELECTRICAL COMA THERAPY. HARRY F. DARLING, J. Nerv. & Ment. Dis. **100**:70 (July) 1944.

Darling believes that the best results in avoiding skeletal fractures as complications of electric coma therapy are to be obtained by allowing the limbs to convulse freely rather than by applying manual or mechanical restraints. More than 350 courses of treatment have been given with this method without direct or indirect fatality or fracture. Since no attempt is made to impede the freedom of action of epileptic patients during their seizures, the attempt to restrain persons with artificially induced fits seems unwarranted.

CHODOFF, Langley Field, Va.

Congenital Anomalies

FAMILIAL CEREBRAL DEGENERATION WITH CORTICAL ATROPHY. H. M. KEITH, Proc. Staff Meet., Mayo Clin. **18**:499 (Dec. 15) 1943.

Keith performed encephalographic studies on 2 infant siblings. Gross encephalic abnormalities were observed; therefore a diagnosis of diffuse cortical atrophy with progressive mental retardation was made for both infants.

GUTTMAN, Philadelphia.

A CASE OF PARTIAL CONGENITAL HEMI-HYPERTROPHY. A. HUSE, J. Neurol., Neurosurg. & Psychiat. **7**:30 (Jan.-April) 1944.

Huse reports the case of a feebleminded man, aged 39, who showed enlargement of the entire left side of the body, involving both osseous and muscular tissues. The hypertrophied left side was weaker than the right. The condition was associated with signs of Recklinghausen disease. The author concludes that two congenital anomalies were present and that the mental deficiency was either idiopathic or secondary to the congenital anomalies.

N. MALAMUD, Ann Arbor, Mich.

CYCLOCEPHALON AND HYPERTROPHIED STRUCTURES IN THE BRAIN OF A CHILD WITH MULTIPLE FACIAL MALFORMATION. JULIO ARANOVICH, Rev. neurol. de Buenos Aires **8**:312 (July-Sept.) 1943.

A male child died on the seventh day of life, with hyperthermia. Except for congestion of the liver, spleen and lungs, autopsy revealed nothing abnormal in the internal organs. Microcephaly, microphthalmia on the left side and multiple chondromas of the face were present.

Macroscopic examination of the brain showed pronounced malformation of both cerebral hemispheres. They formed a large, single vesicular structure, with absence of fissuration and depressions on the lateral surfaces in the region of the sylvian fissure. There was slight indentation at the anterior extremity of this vesicle, at the site of the interhemispheric fissure.

At the base there was typical arhinencephaly, with absence of the olfactory bulbs, nerves and tracts; there was only one ventricle and no corpus callosum; a diverticulum from the roof of the third ventricle pushed the anterior part of the vermis posteriorly; the pyramidal tracts were entirely absent; the anterior part of the vermis and the dorsal nuclei of the thalamus were poorly developed; there was complete absence of the optic radiations and olfactory pathways; the cerebral cortex was arrested in development, the stage corresponding to that usually seen in the second month of fetal life; there was complete absence of association, commissural or projection fibers in the cerebral cortex; the region of the cornu ammonis was the most normally developed part of the brain on either side, and the olives, red nuclei and hypothalamic region were hypertrophied.

The author believes that arrest of development of the neoencephalon permitted inordinate growth of paleoencephalic structures. He postulates a disturbance in circulation of the cerebrospinal fluid in the first to the third month of fetal life to account for the bulge in the roof of the third ventricle and the arrested development of the cerebral cortex.

SAVITSKY, New York.

Encephalography, Ventriculography, Roentgenography

VENTRICULAR CHANGES AFTER CLOSED HEAD INJURY. H. DAVIES and M. A. FALCONER, J. Neurol. & Psychiat. **6**:52 (Jan.-April) 1943.

Davies and Falconer report the results of pneumoencephalographic studies in 100 cases of closed head injury. The cisternal route of injection was used in preference to the lumbar, and only small quantities of air (30 to 60 cc.) were injected. The diagonal width of the body of the ventricle was used as a criterion of the size of the lateral ventricle, a diameter of more

than 2 cm. or a difference of 2 mm. between the ventricles being considered abnormal. A series of 50 controls were studied for comparison. Enlargement of the ventricles, either focal or generalized, unilateral or bilateral, was found in 69 of the 100 cases. The frequency of such dilatation tended to increase with the severity of the trauma, as measured by the duration of post-traumatic amnesia or the presence of blood in the cerebrospinal fluid. Ventricular enlargement first appeared within two to three weeks after injury and reached its maximum within a month. The dilatation, especially of the focal type, was less influenced by the site of the direction of the violence than by the presence or absence of localized fracture of the skull. There was in the majority of cases a close correlation between the clinical signs and the encephalographic changes. This was most striking in cases with residual signs of pyramidal involvement on one side of the body, in which the contralateral ventricle was usually dilated. In cases of post-traumatic intellectual deterioration the ventricles were also frequently enlarged. However, post-traumatic syndrome, post-traumatic epilepsy, signs of primary involvement of the hypothalamus and brain stem and cranial nerve palsies were usually not associated with ventricular dilatation. Thus a normal encephalogram does not rule out permanent organic damage. The authors do not attach significance to nonfilling of the ventricles with air. The mechanism of ventricular dilatation appears to be due to intracerebral atrophic processes resulting either from a focal traumatic lesion or from a generalized vascular disturbance rather than from obstruction to the cerebrospinal fluid pathways.

MALAMUD, Ann Arbor, Mich.

Diseases of Skull and Vertebrae

INJURIES OF THE FACIAL PORTION OF THE SKULL IN WARTIME AND IN PEACETIME. F. SPECHT, München. med. Wchnschr. **89**:391 (May 1) 1942.

Specht emphasizes that the facial portion of the skull encloses a complex cavity which is of considerable functional importance. The rhinologist should make the diagnosis and decide on the treatment. Intracranial complications and septic conditions may result from nasal infection under normal circumstances and even more frequently after injuries. Early prevention of adhesions and of obstruction of the accessory cavities is of the greatest importance. Recovery in cases of severe osteomyelitis originating from accessory cavities may be obtained by radical surgical intervention. Immediate correction is more simple and less dangerous. Internal healing may be obtained only by rhinologic methods. Involvement of adjacent or of more distant organs should be kept in mind. Fractures of the basal part of the skull with aural involvement are frequent. There are also less common paths of infection, such as the subperiosteal abscess of the temporal bone or of the zygomatic arch resulting from suppuration of the middle ear. Whether or not the injured patient will get the correct treatment depends on competent organization, which, however, need not be of vital importance provided the physician who is first called will consult with all the specialists concerned as soon as possible.

J. A. M. A.

Society Transactions

CHICAGO NEUROLOGICAL SOCIETY

RALPH E. HAMILL, M.D., *in the Chair*

Regular Meeting, Oct. 10, 1944

Degeneration of the Basal Ganglia Due to Chronic Carbon Disulfide Poisoning in Monkeys. DR. RICHARD B. RICHTER.

Four monkeys (Macaca mulatta) were repeatedly exposed to carbon disulfide vapor over periods of three hundred and sixty-four to seven hundred and thirty-six days. Acute intoxication was avoided. All the animals manifested signs indicative of profound cerebral damage. These were interpreted as chiefly extrapyramidal in origin. Most striking were certain motor disturbances common to all of the monkeys. The animals became progressively inactive; mimetic facial movements disappeared, and many reactions of orientation, flight and defense were lost. Walking and climbing became slow, difficult and incoordinated, without actual paralysis. The head, trunk and extremities assumed postures of extreme flexion with plastic rigidity. Pronounced action tremors appeared in all animals, and tremor of the resting extremities was present in 1 animal. There were impressive resemblances to the akinetic-rigid syndrome of parkinsonism.

Pathologically, the essential changes in 3 of the animals were massive necrobiotic lesions, symmetric on the two sides and confined strictly to the globus pallidus and the substantia nigra. These had destroyed virtually all the pallidum and the zona reticulata of the substantia nigra. In the fourth animal there were numerous scattered destructive lesions in the corpus striatum and the pallidum, as well as in the substantia nigra.

The pathogenesis of the lesions and their relation to the animals' symptoms and to certain cases of chronic carbon disulfide poisoning in man were discussed.

DISCUSSION

DR. FREDERICK HILLER: Dr. Richter is to be congratulated on this splendid experimental work. On seeing his instructive slides, I was reminded of what I described about twenty years ago as the effect of carbon monoxide poisoning on the human brain. Symmetric necrosis of the pallidum is regarded as a typical effect of such poisoning. This necrosis is not limited to the pallidum but, among other sites in the brain, is also found in the substantia nigra, where the lesion is more or less limited to the so-called red, or reticular, zone. I wonder whether Dr. Richter found this to be true in his experimental animals.

The predilection of the necrosis for certain areas of the brain has puzzled all who have examined the brain in cases of this type. My associates and I were inclined to attribute this predilective localization to a vascular factor, although we did not feel quite satisfied in pronouncing specific circulatory disturbances as the exclusive basis of the pathoclisis in this condition. It is, of course, difficult to deduce from an advanced stage of necrosis whether stasis or some other circulatory failure has caused the cerebral lesion, which presents all the characteristics of tissue necrosis, with vast numbers of gitter cells and predominantly mesodermal repair. In his experiments, Dr. Richter has been in the much more favorable position of seeing the initial stages of this reaction of the brain. I should like to ask whether he has formed any conclusions about the nature of this type of encephalopathy.

DR. VICTOR E. GONDA: The gross pathologic changes localized almost entirely in the striatal system have been mentioned, as well as the minor alterations, which were rather widespread. May I ask whether any changes were seen in the cortex, especially in the so-called motor and premotor cortex?

My second question is a purely theoretic one. Does Dr. Richter think that, under the same experimental conditions, higher apes would show more outward manifestations of the parkinsonian syndrome than monkeys?

DR. GEORGE B. HASSIN: The changes so well presented by Dr. Richter, which he classified as necrosis and which I should prefer to call softening, are not specific for carbon disulfide poisoning, for they may accompany poisoning with other substances, especially carbon monoxide. A definite diagnosis from the microscopic examination alone is thus not possible. I was glad to hear that Dr. Hiller is giving up his vascular theory of the changes associated with carbon monoxide poisoning, a hypothesis advocated also by Spielmeyer and his followers. Dr. Richter's slides showed that the condition of the blood vessels, many of which appeared newly formed, could not be held responsible for the scattered, diffuse alterations in the brain. The changes are most likely due to a direct action of the poison on the ganglion cells, glia, nerve fibers and blood vessels. They seem to involve the peripheral nerves. Probably because of lack of time, Dr. Richter did not mention the changes, if any, in the cortex. It seems that with carbon disulfide poisoning, as with any other type of poisoning, the entire nervous system is involved, the basal ganglia being affected more than any other portion.

DR. R. P. MACKAY: The striking feature of this work is undoubtedly the close resemblance between the pallidal degeneration in these cases of carbon disulfide poisoning and that seen as a result of exposure to carbon monoxide. It is generally admitted that carbon monoxide produces its effects by inducing anoxia. If one places an animal under 5 atmospheres of oxygen, one may saturate the blood with carbon monoxide without damaging the brain, since sufficient oxygen is carried in solution in the blood plasma for the needs of the animal. This being true, it behooves one to ask whether the changes following carbon disulfide poisoning may not also be due to anoxia.

Did Dr. Richter study the oxygen content of the blood in his monkeys or carry out other observations on the ability of the blood to carry oxygen? Conceivably, carbon disulfide, a fat solvent, might dissolve the envelope of the red blood cell and destroy the hemoglobin.

DR. RICHARD B. RICHTER: In answer to Dr. Hiller: These preparations do not resemble the pathologic effects of experimental carbon disulfide poisoning previously described in other species, except in 1 cat of Ferraro's, in which the lenticular nucleus was reported to be necrotic. What they do resemble, almost exactly,

are the necrotic lesions of carbon monoxide poisoning in man, those of experimental carbon monoxide poisoning in dogs and the necrotic areas described by Hurst in the cortex, subcortical white matter, cerebellum and basal ganglia of monkeys after repeated sublethal doses of potassium cyanide. Although the period of intoxication in the animals was prolonged, the lesions themselves are relatively acute and appear to have developed as the cumulative effect of repeated small insults, from which finally the tissues could not recover.

I do not think this material offers the answer to the nature or pathogensis of these, or similar, toxic degenerations or necroses. The completeness of the necrosis and the presence of proliferation and other vascular changes within the lesions themselves suggest a vascular origin. But there are other considerations which speak strongly against such a mode of development. The complete absence of vascular alterations, even of engorgement and stasis, in all other areas of the brain does not support the theory of either structural or functional vascular pathogenesis. Furthermore, it is inconceivable to me how lesions which exhibit such perfect symmetry as these do, and are so exquisitely selective for certain gray structures, could depend on vascular changes. For instance, in the 1 animal in which the corpus striatum was affected, there was pronounced destruction of the small bridges of gray matter which unite the caudate nucleus and the putamen across the internal capsule without the capsule itself being affected in the least. How a vascular lesion could be as selective as that is difficult to understand. The material appears to fit Vogt's concept of general pathoclisis—only this means very little. Whether the preeminent vulnerability of the globus pallidus and substantia nigra is a vulnerability to carbon disulfide as such or to anoxia, or whether it is concerned with effects on respiratory enzymes in the nerve cells is not known.

It is of great interest that, just as in Dr. Hiller's case of carbon monoxide poisoning with damage to the substantia nigra, it was the zona reticulata of the substantia nigra which showed the predominant damage.

In reply to Dr. Hassin: The brains of all these animals were examined in serial sections from the frontal to the occipital pole. In all there was some degree of cellular change in the cortex of the frontal lobes, especially in their most rostral parts. Even these small changes were not seen in the motor cortex or caudal to it. I do not believe that this relatively insignificant amount of neuronal damage was functionally significant, at least not for the motor syndrome exhibited by the animals.

Toxoplasma Encephalomyelitis: A Clinical Pathologic and Experimental Study. Dr. Douglas Buchanan and Dr. Carlos Lara-Gonzales.

1. A clinical report was given of 8 cases of Toxoplasma encephalomyelitis with chorioretinitis.

2. A pathologic report was given of 3 cases in which autopsy was done.

3. The history of recognition of this disease in man was reviewed.

4. The clinical picture of this disease in its prenatal, infantile and adult forms was described.

5. Attempts to cultivate the organism were reported. Experimentally, it was found possible to culture the toxoplasma on the allantoic membrane of fertile hens' eggs and to pass the organism through six generations. It was found impossible to culture the organism on any truly artificial medium.

Attempts were made to produce a pure culture of the toxoplasma from the peritoneal exudate obtained from infected mice. Methods of controlled sedimentation and controlled centrifugalization were employed, but these failed.

Attempts were also made to culture the organism by control of the p_H of the infected suspension with various chemical agents, but these attempts failed. These experiments were carried out with the hope of producing a pure culture of toxoplasmas which could then be used in a cutaneous test for evidence of the infection in man.

6. Studies were made of the life cycle of the organism; mice, rabbits, chickens, ducks and hamsters were used. When these animals were given intraperitoneal and/or intracerebral injections of the toxoplasma, no evidence of the organisms in the peripheral blood was found at any time before the animal's death or its recovery.

When the toxoplasma was injected intravenously, a few organisms were observed in the peripheral blood of 4 mice just before death. In all the other animals no organisms were found at any time before the animal's death or recovery. The peripheral blood of these animals was examined by direct smear every three hours until death or recovery. Although evidence of the toxoplasma was found in the peripheral blood in only 4 mice, the organism was noted in the organs of all the animals after death. In addition, transmission of the disease to other groups of animals was obtained with suspensions of these organs.

7. The present method of testing human serum for the presence or absence of neutralizing antibodies to the toxoplasma was described.

8. The significance of this disease in the production of spastic quadriplegia, mental retardation and convulsions was pointed out.

DISCUSSION

Dr. George B. Hassin: I think this form of encephalitis was present in a newborn infant, a twin, who died fifteen days after birth. I did not have a good history, but I obtained the brain and demonstrated the pathologic findings before this society (Acute [Epidemic?] Encephalitis: Report of a Case in a New-Born Twin with Histologic Observations, Arch. Neurol. & Psychiat. **18**:44 [July] 1927). The usual changes seen with encephalomyelitis were present; in addition, there were peculiar bodies, the nature of which I did not understand. Under the influence of the work of the British neuropathologist, De Fano, I classified them as "minute bodies." Some are single; others are clumped together and are, in my opinion, identical with the formations described twelve years later by Wolf and Cowen and subsequently identified by them as toxoplasmas. I sent photographs of my histologic specimens to Dr. Abner Wolf and Dr. Sabin, who could not commit themselves without seeing the slides. These I could not send, as they mysteriously disappeared, together with the gross material. Dr. Buchanan rightly stated that the micro-organisms obtained in cultures and in experimental work differ from those seen in histologic specimens, and he probably can help me in identifying them in my slides. I think my case was one of toxoplasmic encephalitis. I was particularly interested in this case as the disease occurred in a twin, while the other twin and the mother remained well. A similar case in a twin was recorded by Zuelzer (Infantile Toxoplasmosis, with Report of Three New Cases, Including Two in Which the Patients Were Identical Twins, *Arch. Path.* **38**:1 [July] 1944).

DR. PETER BASSOE: Within the last three weeks I have seen 2 adults with chorioretinitis close to the optic disk. An ophthalmologist diagnosed the condition as the "juxtapapillitis" described by Jensen in 1908. I looked up this article, and the picture was similar to that in the case Dr. Buchanan described. I also looked up other articles on Jensen's disease, and all state that no satisfactory cause has been found. There have been guesses, but no proof, that tuberculosis, syphilis and other conditions are responsible. Perhaps the toxoplasma is the answer.

DR. VICTOR E. GONDA: I had an opportunity to study roentgenograms of the skulls of 2 children between the ages of 1 and 2 years in which extensive calcifications were shown. These calcifications are considered so characteristic of the disease that their presence constitutes verifications of the diagnosis of toxoplasma encephalitis. Will Dr. Buchanan interpret these observations?

DR. DOUGLAS BUCHANAN: I agree with Dr. Hassin that the organisms in his case were toxoplasmas; those at 7 and 11 o'clock I could not identify.

Of our 63 patients who had had trouble with their eyes and whose serum gave positive reactions for the toxoplasm, and, in addition, of 11 patients who presented the complete picture of toxoplasmosis, only 1 showed calcifications in the skull. However, these were in a unique position; all appeared to be in the posterior part of the brain. This localization is used in the differential diagnosis of toxoplasmosis and tuberous sclerosis.

Causalgia: A Preliminary Report of Nine Cases in Which Treatment with Surgical and Chemical Interruption of the Sympathetic Pathways Was Successful. CAPTAIN I. JOSHUA SPEIGEL and CAPTAIN JACK L. MILOWSKY, Medical Corps, Army of the United States.

From an analysis of the clinical picture and of the results following treatment of 9 patients with causalgia observed by the authors in an unselected series of 275 men with peripheral nerve injuries, the following conclusions were drawn:

1. The syndrome followed injury to all or any of the major nerves of the upper extremity. In spite of numerous injuries to the veins of the lower extremity, only 1 case of causalgia involving the leg occurred.

2. Injury to a blood vessel frequently accompanies nerve injuries in cases of causalgia but is not a necessary concomitant of nerve injury in the production of pain.

3. The most constant symptom of causalgia is hot, burning pain, aggravated by movement and friction.

4. The most constant finding is shiny, cold, profusely perspiring and frequently cracked skin in the extremity involved, with hyperesthesia occurring in most cases. Roentgenographic evidence of decalcification of the involved extremity is frequently seen.

5. The pain does not appear to be due to continuous irritation by a scar or a foreign body.

6. The degree and quality of pain are in no way commensurate with the type and extent of injury.

7. The area of sensory deficit does not delineate the area of pain, but the two frequently shade into each other.

8. Personality disorders and hysteria are the result rather than the cause of causalgia.

9. Neurolysis is not a useful procedure in the treatment of causalgia per se, although it may be necessary in treatment of the specific nerve deficit.

10. It is injudicious to subject the patient to a series of operations ranging through neurolysis, nerve section and periarterial sympathectomy before attempting chemical and surgical interruption of the sympathetic pathways.

11. Interruption of the sympathetic pathway, temporarily, by sympathetic block, or permanently, by surgical sympathectomy, is a highly dependable form of treatment for causalgia. In case of the upper extremity, it is not necessary to remove the stellate ganglion for effective control of the pain.

12. Sympathectomy should not be performed until a series of diagnostic sympathetic blocks has proved the efficacy of interruption of the sympathetic pathway.

13. Occasionally the pain of causalgia can be more or less permanently controlled by sympathetic block with local anesthesia when sympathectomy, for other reasons, is not feasible. Alcohol block, in selected cases, is a useful procedure.

It is concluded, therefore, that sympathetic block by chemical or surgical means is a highly satisfactory method of treatment for causalgia and should occupy a prominent position in the therapeutic procedures of those whose function it is to treat this complaint.

DISCUSSION

DR. GEZA DE TAKATS: I congratulate Dr. Spiegel on this series. A few points should be emphasized. One should never consider doing a sympathetic ganglionectomy unless a sympathetic block is successful. A certain group of patients responds favorably. When the patient is seen early, sympathectomy, repeated sympathetic blocks combined with physical therapy or preganglionic sympathectomy is effective. But a time element militates against this procedure. Most of the patients seen after industrial accidents come years later, having consulted industrial surgeons, orthopedic surgeons, neurologists and so on. By the time they get to some one who can take care of them, they have been in splints for intractable pain; they have an addiction to morphine, and a syndrome has developed in which the continuous pain has stamped a pattern on the cortex. Interruption of peripheral nerves does not help this syndrome; and, while sympathetic block and sympathectomy are of value in the early stages, there comes a time, as Dr. Speigel has mentioned, when such treatment is not effective.

The second point is that there is a difference between the "hysterical hand" and the causalgic hand. The "hysterical hand" never shows any vasodilatation; if anything, it is cool, whereas the causalgic hand shows vasodilatation, which is certainly due to secretion of painful substances at the nerve endings. Why does sympathetic block or sympathectomy help when, obviously, the sympathetic nervous system has not been injured? Further work is necessary on this point.

This paper is stimulating, and I hope it will make every one feel the importance of treating these patients early.

DR. I. JOSHUA SPEIGEL: I wish to thank Dr. de Takats for his discussion. I should like, also, to reiterate one point: One should never think of performing a surgical sympathectomy without a repeated series of chemical blocks to determine whether or not it will be efficacious. I might add that chordotomy in cases of severe causalgia has not always been attended by relief of pain. Certainly, it is dangerous to try such a procedure in a case in which the cortical pattern of pain has already

been implanted. Of course we were fortunate. Our patients were young, and all the injuries were comparatively recent. The patients with long-standing causalgia, who have been permitted to stay in casts because of pain, are exceedingly difficult to treat. It is precisely for this reason that this paper is presented—to point out that direct chemical or surgical attack on the sympathetic nerve chain should be instituted early if a complete remission of symptoms is to be obtained.

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

PAUL I. YAKOVLEV, M.D., *Presiding*

Regular Meeting, Oct. 19, 1944

Mental Deficiency as a Community Problem. DR. RANSOM A. GREENE, Waltham, Mass.

Close to 2 per cent of the total population falls within the limits of the definition of mental deficiency. Thus, in Massachusetts there must be about 100,000 people who are feebleminded. Of these, only about 10,000 are registered with the state and other public agencies and are known as feebleminded. Some 90,000, therefore, remain outside the official record. They represent a largely negative factor in the economic and political structure of the community. Of persons recorded as feebleminded, only about 5,000, or approximately 5 per cent of a total feebleminded population of the state, are in the institutions for the mentally defective. The Walter E. Fernald State School provides for 2,000 of them. There are between 5,000 and 6,000 persons who are recorded as feebleminded and should be in institutions but who remain in the community, in the care of their families and various social agencies. Some mental deficiency is preventable. The prevention is largely a matter of medical research in the field of mental deficiency. In a large proportion of cases idiocy and imbecility are due to preventable factors, such as prenatal hazards to maternal health, birth injuries, infections, nutritional deficiency and diseases of the brain in infancy and early childhood. To a considerable extent, moronity, inherited through defective germ plasm, is perhaps also preventable by eugenic measures. Yet feeblemindedness will still be produced by the unpredictable, and therefore nonpreventable, vagaries of transmission in the germ plasm of latent hereditary traits from apparently healthy and well endowed parents to some of their less fortunate offspring; and there will also always be persons who become disqualified for normal living and fall from borderline normal intelligence to the moron level as a result of the ever increasing dependence of modern man's social adjustment on his intelligence.

DISCUSSION

DR. WILLIAM G. LENNOX: The other day I read an article by Prof. L. H. Snyder, of Ohio, who has done a great deal of work on heredity. His experiments have shown that when the blood of one parent is negative for the Rh factor and that of the other is positive, feeblemindedness occurs in the children with unusual frequency. This factor contributes to clotting of the blood and causes damage to the brain. I wonder whether Dr. Greene has any information on this point.

DR. BRONSON CROTHERS: I should like to ask Dr. Greene what is his borderline between psychosis and feeblemindedness. I want to find an administrative criterion for the selection of children who can be handled in this school and those who cannot be handled in any institution for the feebleminded.

DR. RANSON A. GREENE, Waltham, Mass.: While heredity is a strong factor in mental deficiency, environment is also important. I know from available figures that in 1900 the average span of life in the United States was 49 years. In 1944, according to figures of insurance companies and to the statistics of the United States Bureau of the Census, the average span of life was almost 72 years. This means not only that the life span of healthy and well endowed people is increased, but that many who are potentially or actually feebleminded at birth are being salvaged. I wonder whether this does not mean that there is being salvaged a group of persons who will have to be cared for in an institution or carried around on a pillow just because they are alive. This group is increasing. The obstetricians and the pediatricians may be responsible in a measure for some of this. I think they should take into account certain factors that they have not considered seriously. I believe that a great deal of preventable mental deficiency results from environmental factors and that when more is learned about the causation of mental deficiency, it will be found that the most important factors are environmental, rather than hereditary.

In reply to Dr. Lennox' question about the Rh factor: I have read quite a bit on the subject, but I do not know much about it personally. I think it is a matter for research, which will lead somewhere in differentiation of what are hereditary and what are environmental influences. Many conditions probably involve both.

Dr. Crothers' question was pertinent and difficult. There is only one way I can answer it. This institution, which in three years will be 100 years old, was built and intended primarily for the care of the feebleminded, to educate them to the capacity of their intelligence. That is what it has always attempted to do. But as years have gone by, more and more applications are received for admission of children who are not capable of any measure of elementary scholastic or occupational training because their mental deficiency, obvious as it may be, is associated with a gross disorder in the development of their behavior pattern. The mental deficiency of these children is wholly a secondary problem. The major problem is the pattern of their behavior. Because of this, not only are they incapable of any measure of elementary scholastic and occupational training in a school for the feebleminded, but their presence in the group of trainable feebleminded children destroys the very purpose for which the school is primarily intended. Either this institution trains the feebleminded, or it cares for psychotic children who happen to be feebleminded as well, or who become deteriorated, i. e., demented. The latter task cannot be carried out on the plane of training for which the school was built. It is the task of a psychiatric hospital for children. There are feebleminded children who are also psychotic. They are noisy and destructive and will have to be cared for as long as they live. A certain number of morons as they grow older have dementia precox, or they had the disease primarily. They are not suitable for admission to an institution that cares for feebleminded children and expects to send at least some back to their homes or communities. One cannot send a psychotic and feebleminded child back to the community. Some of these psychotic children may be recognized as such in early childhood. There are no provisions for

their care at this school. They must go to a psychiatric hospital. There is no place in Massachusetts where a child with a psychosis can be cared for. I have begged for years for such an institution. Attempts have been made to care for them in some mental disease hospitals, but that does not work. Having been the superintendent of a psychiatric hospital myself, I know that it cannot be done. There should be a special place for the care of psychotic children.

Clinical Aspects of So-Called Mongolian Imbecility. DR. CLEMENS E. BENDA, Wrentham, Mass.

Among the various types of mental deficiency, mongolism is outstanding, for two main reasons: It is not due to hereditary factors and may therefore occur potentially in normal families; and, second, mongolism furnishes one of the most interesting illustrations of the way in which normal development can be influenced by abnormal environmental factors during the period of gestation.

In a recent study at the Boston Lying-in Hospital, Dr. Berkeley Beidleman found that a diagnosis of mongolism has been made in 42 cases since 1930, a figure which represents an average of 3.4 per cent of the births at that hospital for that period. Earlier estimates showed that mongolism occurs in at least 2 per cent of the births in the population, an incidence which certainly deserves the attention of members of the medical profession.

A study of the growth disorder after birth indicates that the child with mongolism lacks normal function of those glands which guarantee normal growth and maturation. There is evidence of hypofunction of the thyroid and the gonads and, to a minor degree, of the adrenal cortex. The pathologic changes suggest lack of thyotropic, gonadotropic and adrenocorticotropic hormones; this leads to the conclusion that the pituitary gland, which regulates these functions, is essentially at fault. From a study of the pituitary glands of more than 40 patients with mongolism evidence has accumulated that the pituitary of children with this condition is abnormal in many ways. It is beyond the scope of this presentation to discuss the abnormality of the pituitary in more detail.

It is evident, however, that the mongolian imbecile is born with mongolism and that the dysfunction of the pituitary is only part of the general developmental deficiency. The abnormality of the heart, so frequent in cases of mongolism; the pathologic changes in the vascular system; the abnormal lines in the hands, and many other factors indicate that the fetus was exposed to noxious factors during many months of the period of gestation and that the abnormality of pregnancy started soon after the impregnation of the ovum. The pathologic changes indicate a hormonal deficiency of the mother during pregnancy.

Studies were made on 250 mothers of children with mongolism, a number which has now been increased to more than 300, and the results checked by Dr. Beidleman, in his observations on the material of the Boston Lying-in Hospital. The results indicate that the mothers of these children were not in proper condition for pregnancy when they carried the child who proved to be a mongolian imbecile. Bleedings, abortions, prematurity and other factors indicate that mongolism occurs on a threshold of hormonal sterility. It is suggested that either the function of the corpus luteum or that of the pituitary is at fault during the specific pregnancy. A study of the factors producing the deficiency indicates that physiologic factors, such as age, or several pathologic conditions, such as illness, exhaustion and immaturity, may produce the temporary threshhold of sterility.

DISCUSSION

DR. BRONSON CROTHERS: Dr. Benda suggested that attempted abortion might produce mongolism. How early in the course of pregnancy would this have to occur? It seems to me that mongolian imbeciles are much alike.

DR. AUGUSTUS ROSE: By the threshold of sterility does Dr. Benda mean a physiologic or a pathologic condition of the mother?

DR. D. DENNY-BROWN: It is remarkable that the mongolian imbecile preserves a juvenile appearance, and thus differs notably from a child with progeria. If pituitary insufficiency is responsible for progeria, the thickness of the eyelids and the absence of wrinkling of the skin in mongolism would require additional explanation.

DR. BRONSON CROTHERS: On the theory that mongolism is an endocrine disorder, has Dr. Benda any explanation of such defects as congenital heart disease and congenital cataract?

DR. WILLIAM O. LENNOX: Does a woman ever have two mongoloid children? Does endocrine therapy offer any hope?

DR. CLEMENS E. BENDA, Wrentham, Mass.: In answer to Dr. Crothers' question about the time at which an abortion, or an attempted abortion, must occur to produce mongolism: My material includes several instances in which the child with mongolism was in the middle of a series of normal siblings. These cases appeared entirely unexplained. When I inquired into the circumstances of the pregnancy, several mothers told me confidentially that when they missed their first menstrual period, they took pills obtained from a drugstore to induce menstruation.

Another point worth noting is that in other cases of mongolism menstruation continued during the first three months of pregnancy, an indication that something was wrong with the mechanism of pregnancy. In a third group of cases a history of threatened abortion in the third month was given.

In regard to Dr. Crothers' question about congenital heart disease and congenital cataract: My theory is that all such deficiencies indicate a pathologic period of gestation. I think that the infantile development of the heart and vascular system of mongolian idiots is an indication of a general growth deficiency in fetal life. More recent research on cataract has produced evidence that congenital cataract is associated with various endocrine disorders of the mother or with infectious diseases during pregnancy.

Dr. Rose asked about the pathologic condition of the mother in relation to the threshold of sterility. My observations indicate that many mothers have difficulty in becoming pregnant, in spite of a desire to have children. Sometimes they have tried from five to ten years to have a child; and when they finally succeeded, the child was a mongolian imbecile. This has led me to suspect a hormonal deficiency of the mother, which may be related to inadequate function of the corpus luteum.

As to the offspring of persons with mongolism, there is no report in the literature which provides indubitable evidence that a woman with mongolism has borne a child. The only such report comes from an English source, but it is not accompanied with pictures and there is no proof that the woman under consideration really had mongolism. There are a number of people of East

European stock who have mongolian characteristics, and a feebleminded woman with these characteristics might easily be thought to have mongolism. I studied more than a dozen ovaries of women with mongolism, and in no case was there evidence of mature graafian follicles.

In answer to Dr. Denny-Brown's question about the relationship of mongolism and progeria: I am not able to give any facts. I have seen several cases in which premature aging was recognizable in young adults as a symptom of progressive deterioration; but I have seen only 1 case of true progeria, and I am not familiar with the details of the endocrine disturbance in that case.

In answer to Dr. Lennox, we have seen a few cases of 2 and 1 case of 3 mongolian imbeciles in one family. Such an occurrence is rare, however, and I should not hesitate to encourage a mother, if she is young enough, to have another child after having borne a mongolian imbecile.

Achondroplasia of Parrot and Marie and Familial Osteochondrodystrophy of Morquio: Demonstration of Patients. DR. LAWRENCE BOWSER, Waltham, Mass.

Three patients with the typical achondroplasia of Parrot (1872) and a sister and brother with familial osteochondrodystrophy, described by Morquio (1929), were presented and compared. The cases of the sister and brother were reported by Drs. Farrell, Maloney and Yakovlev (Morquio's Disease Associated with Mental Defect, ARCH. NEUROL. & PSYCHIAT. **48**:456 [Sept.] 1942). Familial osteochondrodystrophy has often been mistaken for achondroplasia; yet on comparison of these two types of dwarfism due to disorders of osteogenesis, the difference is striking. Aside from the fact that osteochondrodystrophy is a familial disease, several siblings being affected, although others in the same family may be normal, the skeletal abnormalities in this condition are of a different type and distribution than those seen in achondroplasia. In the latter condition the dwarfism is due to premature ossification of the epiphysial cartilages of the long bones of the extremities, while the vertebral column and the axial skeleton show fairly normal growth and development. Thus, the trunk is long; and except for exaggerated sacrolumbar lordosis, the vertebral column is abnormally erect. The back of the patient is usually flat. In achondroplasia the dwarfism is chiefly appendicular. The long bones of the proximal segments of the extremities —humerus and femur—are conspicuously shortened. The condition is evident at birth and is even recognizable in the fetus. It was known to obstetricians long before it was differentiated as a clinical entity in the adult.

Familial osteochondrodystrophy is not evident at birth. The condition apparently reveals itself at the end of the first year of life, progressing during early childhood and then becoming fixed. The axial skeleton is predominantly affected. The dwarfism is due chiefly to the stunting of growth and the deformation of the vertebral column, thorax and pelvis. The large proximal joints—iliofemoral and scapulohumeral—show a want of osteogenesis associated with an actual destructive process in the cartilage and bone. The roentgenograms reveal a characteristic picture, especially in the pelvis, which is usually narrow; the acetabulum is small and shallow, and the head of the femur is small and often eroded. Usually a subluxation of the joint is present bilaterally. The gait of the patients is greatly impeded thereby and is highly characteristic. The outstanding features are the shortness of the trunk and, especially, of the neck; thus, the head appears sunken between the shoulders, the chin resting on the sternum. The dorsal kyphoscoliosis, the forward protrusion of the sternum and the collapse of the thoracic cage are characteristic.

Mental deficiency is frequent in cases of achondroplasia. In fact, it appears that most persons affected are below par mentally. In cases of Morquio's disease thus far reported the mental deficiency does not figure prominently in the clinical picture. It is likely, however, that as physicians become more familiar with this form of familial dystrophy, the mental defect will be more frequently recognized in these patients.

DISCUSSION

DR. RUDOLPH NEUSTADT: Three and one-half years ago I examined the urine of these 2 patients with Morquio's disease. Edward's showed complete lack of androgens, while Josephine, at that time 18, had an insufficient amount of androgens but a normal amount of estrogens. I am curious to know whether she menstruates.

DR. PAUL I. YAKOVLEV, Waltham, Mass.: Yes, she does. Apparently, neither she nor her brother show any gross hormonal disturbances except that both are retarded in sexual maturation. Both, however, have a low calcium content of the blood. In this, again, they differ from achondroplastic dwarfs.

DR. CLEMENS E. BENDA, Wrentham, Mass: Is Morquio's disease a true malformation?

DR. PAUL I. YAKOVLEV, Waltham, Mass.: Nothing is known of the pathogenesis of this condition, and so the question remains open. There is obviously a familial metabolic disorder, with gross skeletal malformation. Morquio suspected that a neuroregulatory mechanism was involved.

Book Reviews

The Doctor's Job. By Carl Binger, M.D. Price $3. Pp. 423. New York: W. W. Norton & Company, Inc., 1945.

"The Doctor's Job" was written primarily for the laity. It represents an attempt to familiarize them with some of the philosophy of the practice of medicine in the past and at present. As such, it lets some skeletons out of the closet for ventilation. Physicians no longer are represented as God-like, magical creatures with encyclopedic knowledge of all things. Medical ethics, the matter of fees, the problem of the choice of a physician, the advantages and limitations of the family doctor and the role of the specialist are discussed.

Dr. Binger does not believe that magic need be invoked in an intelligent physician-patient relationship. The importance of the transference situation is touched on, and the appeal is for more awareness along these lines and less hocus-pocus.

A review which appeared in the *New York Times* a short while ago stated that the book should have been called "The Psychiatrist's Job." It is true that the book emphasizes the psychiatric implications of all illness. It also presents in some detail the psychosomatic viewpoint, particularly in discussion of peptic ulcer, asthma, hypertension, tuberculosis, etc. The relationship of personality constellation to disease is made relatively simple while remaining good psychiatry.

Dr. Binger is interested, too, in the economic aspects of medical care. Office, hospital and clinic practice are discussed in this frame of reference, and a chapter is devoted to socialized medicine. In general, the views expressed are liberal, yet cautious.

The book has an honest, down-to-earth quality and a fine touch of humor. The psychiatrically trained person will probably learn little from it; the student and general practitioner may learn a great deal, but the book's big contribution is that it should make for a better informed laity, with a healthier conception of the role of their physicians and with some insight into the emotional component of disease.

Peripheral Nerve Injuries; Principles of Diagnosis. By Webb Haymaker, Major, Medical Corps, Army of the United States, and Barnes Woodhall, Lieutenant Colonel, Medical Corps, Army of the United States. Pp. 227, with 225 illustrations. Philadelphia: W. B. Saunders Company, 1945.

War is the time for all good surgeons to come to the aid of the peripheral nerves. Haymaker and Woodhall, in this superbly illustrated small volume, have done a notable service to the surgeon, revising the concepts laid down in the older textbooks of anatomy and surgery and getting away from the static concept that has long been attached to the nervous system. The great collections of cases, clinical records, pathologic tissues and photographs that have been accumulated at the Army Institute of Pathology serve as the basis for the book. Some of the best medical artists in the country have illustrated the text with really lifelike pen and ink drawings. Photographs are abundant.

Section I is devoted to analysis of the segmental and peripheral nerve supply of skin, muscles and skeleton; section II deals with the examination of the peripheral nervous system, and section III discusses injuries of plexuses and peripheral nerves. A fourth section would be desirable but probably cannot be written for years to come. Such a section would deal with restitution and end results of treatment, with serial photographs illustrating the steps of recovery.

The authors have kept their book small in size but large in compass. There are no "case reports," with their irrelevancies and the usual padding. The style is terse, and the illustrations really illustrate.

The Shaping of Psychiatry by War. By John Rawlings Rees, M.D. Price, $2.75. Pp. 158. New York: W. W. Norton & Company, Inc., 1945.

Brigadier John Rawlings Rees, consulting psychiatrist to the British army and medical director of the Tavistock Clinic, London, delivered this material as the Thomas W. Salmon Lectures. He divides his material under four chapter headings, entitled "The Frontiers Extend," "Opportunities Emerge," "The Way Ahead" and "The Tasks of Psychiatry."

Interest in psychiatry was stimulated as a result of World War I, but certainly it has matured more as a result of present war experience than it could have done in years of peace. The author considers the problems of aptitude tests, selection of officer candidates and the study of character stability, personality and leadership. The importance of problems of morale is stressed.

Brigadier Rees emphasizes that psychiatrists, as a result of their war and civilian experience, "have something of value to say in almost every major problem of society—in the planning and maintenance of peace, in the management of nations and in other questions of this magnitude and importance."

In a short appendix, the author outlines the tasks of both military and civilian psychiatry as he envisages the opportunities and responsibilities that lie ahead.

The volume is an illuminating document, full of important data concerning military psychiatric problems. It is highly recommended.

News and Comment

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

At the meeting of the society on May 25, 1944, Paul I. Yakovlev, M.D., president, a symposium was held on the humoral conduction of nerve impulses, and the following papers were read: "Clinical Aspects of Myasthenia Gravis," Henry R. Viets, M.D.; "Electromyographic and Ergographic Studies in Myasthenia Gravis," Mary A. B. Brazier, Ph.D., and "Physiological and Pharmacological Aspects of Neuromuscular Diseases," George H. Acheson, M.D.

Abstracts of the papers with discussions were published in the December 1944 issue of the *Journal of Nervous and Mental Diseases*, pages 613 to 621.

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